*ANNUAL MEETING: LIVERPOOL AND SOUTHPORT, JULY 13—21, 1950*

JUN 14 1950

MEDICAL LIBRARY

# BRITISH MEDICAL JOURNAL

JOURNAL OF THE BRITISH MEDICAL ASSOCIATION

## SATURDAY MAY 27 1950

## TABLE OF CONTENTS

**Observation, Its Meaning and Importance** SIR HENRY SOUTTAR, C.B.E., D.M., M.Ch., F.R.C.S. ..1219

**Intermittent Dosage in the Treatment of Pulmonary Tuberculosis with Streptomycin** J. R. BIGNALL, M.D., M.R.C.P., J. W. CLEGG, M.R.C.S., D.C.P., J. W. CROFTON, M.D., M.R.C.P., B. J. DOUGLAS SMITH, M.B., H. D. HOLT, M.R.C.S., D. A. MITCHISON, M.B., and P. ARMITAGE, B.A. .....1224

**Bornholm Disease** J. H. S. HOPKINS, M.B. .....1230

**Coxsackie Viruses and Bornholm Disease** G. M. FINDLAY, C.B.E., M.D., F.R.C.P., and ELSIE M. HOWARD .....1233

**Abacterial Form of Endocarditis with Necrosis of the Ears** KEITH BALL, M.D., M.R.C.P. .....1236

**Diphtheria in South Persia** R. HODGSON, F.I.M.L.T., and I. S. STEWART, M.B. .....1238

### MEDICAL MEMORANDA

Spontaneous Rupture of Bladder Associated with Unusual Congenital Anomalies. NEIL WARD-MCQUAID, M.B., F.R.C.S. .....1240

Fatal Air Embolism Due to Vaginal Douching in Pregnancy. R. F. COOKE, M.D. .....1241

### REFRESHER COURSE

Congenital Heart Disease—II. MAURICE CAMPBELL, O.B.E., M.D., F.R.C.P. ....1250

### GENERAL ARTICLES AND NEWS

General Practice: A New Perspective 1251

THIRD WORLD HEALTH ASSEMBLY ....1255

REFRIGERATED BONE IN SURGICAL PROCEDURES .....1257

MEDICINE IN 1850: Exhibition at the Wellcome Historical Medical Museum 1258

NOVA ET VETERA .....1259

REPORTS OF SOCIETIES .....1260

A New Type of Foot Support for the Lithotomy Position. G. E. E. USHER-SOMERS, M.R.C.S., L.R.C.P., D.R.C.O.G. 1266

MEDICAL NOTES IN PARLIAMENT .....1275

THE SERVICES .....1276

UNIVERSITIES AND COLLEGES .....1277

MEDICAL NEWS .....1278

BIRTHS, MARRIAGES, AND DEATHS .....1279

QUESTIONS AND COMMENTS .....1281

### MEDICO-LEGAL

No Indecent Advertisement .....1277

Epidemiology Section .....1280

### LEADING ARTICLES

The Training of the G.P. .....1244

Streptomycin Resistance of Tubercle Bacilli .....1245

Towards a Population Policy .....1247

Bornholm Disease and the Coxsackie Virus .....1248

### ANNOTATIONS

Testing the Responses of the Pituitary–Adrenal System .....1249

Khellin in Angina .....1249

### REVIEWS

The Acute Appendix .....1242

Topical Therapy .....1242

Rectal Surgery .....1242

Surgical Treatment of Hypertension ..1242

Management of Obesity .....1243

### OBITUARY

H. Hyslop Thomson, M.D., D.P.H. ....1274

B. A. Peters, M.D., D.P.H. .....1274

### SUPPLEMENT

The Secretary Reports .....229

Cost of Hospital Service—FOOD OR DRUG DEFINED—THE ELDERLY CHRONIC SICK—HOSPITAL STAFF TERMS—DOCTORS' LOW PAY — HOSPITAL STAFF AND NATIONAL INSURANCE .....230

GENERAL MEDICAL SERVICES COMMITTEE 233

MEETING OF MIDDLESEX PRACTITIONERS 234

118th Annual Meeting: Programme ....236

CORRESPONDENCE .....243

ASSOCIATION NOTICES .....244

### CORRESPONDENCE

Intestinal Obstruction Due to Food. G. KEYNES, F.R.C.S.; R. C. ALEXANDER, F.R.C.S.; F. MARSH, M.D. .....1266

Age at the Menarche. D. C. WILSON, M.D., and IAN SUTHERLAND, D.Phil. ..1267

Iodized Salt. J. M. HAMILL, M.D. ....1267

Intravenous Iron. F. S. MOONEY, M.D.; OSKAR J. SLOWIK, M.B. .....1267

Scarlet Fever, Rheumatic Fever, and Nephritis. T. W. BUCHAN, M.B. ....1268

Carcinoma of Stomach. S. LIPETZ, M.D. 1268

Spinal Analgesia for Caesarean Section. SHILA G. RANSOM, M.R.C.S.; STAFFORD MATTHEWS, F.R.C.S.Ed. .....1269

The Medical Bill. J. K. CARTER, M.B.; W. B. MANLEY .....1270

Administration of P.A.S. R. H. P. HICK, M.R.C.S. .....1270

The G.P. at the Crossroads. H. H. SANGUINETTI, D.M.; J. F. PAYAN, M.R.C.S.; THOMAS REES, M.R.C.S. ....1270

Morphine in Acute Chest Infections. E. W. THOMPSON EVANS, M.D. .....1271

Medical Artists. D. H. TOMPSETT, Ph.D. 1271

Mass Vaccination. A. W. FOWLER, F.R.C.S. .....1272

Maternity Service. M. C. STOPES, D.Sc. 1272

British Spas. A. P. CAWADIAS, M.D. ..1272

Brachial Neuralgia. M. G. GOOD, M.D. 1272

Maternity and the N.H.S. G. A. FLANN, M.D.; J. S. TAYLOR, M.B. .....1272

Immunization and Poliomyelitis. MARY E. BUDDING, M.B. .....1273

Rheumatoid Arthritis. J. D. DILLON, M.R.C.S.; C. B. S. FULLER, M.D. ....1273

Tuberculosis and Industrial Injury Benefit. W. SANTON GILMOUR, M.B. 1274

BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON, W.C.1

No. 4664, WEEKLY, PRICE 2/-

*Copyright*

REGISTERED AS A NEWSPAPER

I'm only a vertebrate biped . . .

That's what I am. . . I use my feet for walking, running, climbing and falling down, and I plan to go on using 'em that way for the next eighty or ninety years. They've got to last. That's why my feet are more important than yours — even if they're not so big. Well . . . Clarks make Playe-Ups strong and good, and Clarks Footgauge sees to the fit. So whatever are we waiting for?

* Clarks Children's Sandals are made in several *widths*, and fitted by Clarks Footgauge for length *and* breadth *and* girth.

Clarks SANDALS

# Against exhaustion

The energising and therapeutic effect of glucose is available in a most acceptable form in LUCOZADE.

Whereas ordinary glucose preparations may have a sickly and even nauseating effect on the palate, LUCOZADE is remarkably refreshing. Once tasted — it is never refused.

*An improved form of glucose therapy*

This pleasing characteristic is of the greatest value in treating cases of shock, physical exhaustion and other conditions requiring glucose ingestion.

(Containing Dextrose, Maltose, and Dextrin in solution equivalent to 23% w/v Liquid Glucose B.P.)

**LUCOZADE**

LUCOZADE LTD., GT. WEST RD., BRENTFORD, MIDDX.

M.17

The ability to get about, to maintain daily interests and social contacts, plays an important part in the continued health and happiness of the disabled and the infirm.

For this purpose the NELCO "SOLOCAR" is ideal. Electrically driven; silent, vibrationless and free from fumes; operated with one hand—effortlessly and without strain—it climbs any hill, travels 35 miles without re-charging, turns in its own length.

★ Agents in all parts of the Country.

*The Nelco* **SOLOCAR**

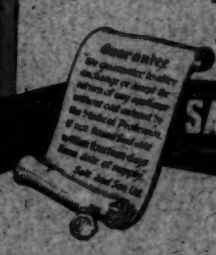
NELCO LTD., STATION ROAD, SHALFORD, Nr. GUILDFORD, SURREY.

M.7

THE "SALTAIR" ARTIFICIAL BREAST

—the obvious solution of the psychological problem which frequently follows breast amputation. It restores the normal figure line, banishes self-consciousness, encourages resumption of normal activities. Can be worn while bathing, as it retains its shape when wet and can be easily dried. Available in the "Saltair" Brassiere or separately for sewing into patient's own foundation garment. Details to doctors on request.

*Appointments at London address: 1 STANLEY HOUSE, 103, Marylebone High Street, London, W.1. Tel.: Welbeck 3034.*



SALT & SON LTD · BIRMINGHAM 2

BRITISH MEDICAL JOURNAL

LONDON SATURDAY MAY 27 1950

# OBSERVATION, ITS MEANING AND IMPORTANCE*

BY

Sir HENRY SOUTTAR, C.B.E., D.M., M.Ch., F.R.C.S.
*Consulting Surgeon, London Hospital*

The Medical Society of London is approaching the second century of its foundation, and the Annual Oration has been given by an unbroken succession of orators for close on 180 years. I am deeply conscious of the honour you have done me in inviting me to share in this distinguished succession and to pay my tribute to the great founders of the society. I feel that I cannot better discharge my debt than by a consideration of that faculty of which they were all supreme exponents, the faculty of observation. Since their day the whole art of medicine has changed and a science of which they knew nothing has claimed it for its own. But still to-day we can admire the clinical insight which could unravel difficult problems unaided, and I would urge that, with all the wonderful resources we possess, the most indispensable resource of all is direct clinical observation.

Consciously or unconsciously we all spend a great part of our lives in observation and we are all agreed on its importance, but we rarely consider the mechanism by which the outside world presents itself to our observation or the mechanism within ourselves by which our observation is effected. Yet surely such an inquiry is essential to any real appreciation of the world around us, for only by such an inquiry can we form any opinion upon how far the apparent world of our experience really exists, how much of it is real, and how much of it is coloured or even created by our own imagination. With the profound philosophical problems involved, with which philosophers have amused themselves since the beginning of history, I do not propose to deal, and indeed I should be quite incompetent to do so. I propose to sketch for you only the physical and physiological mechanisms of observation and perhaps to devote a little time to the consideration of certain practical conclusions.

Our contact with the world and the possibility of our observing depend upon our five senses. Of these, touch demands actual contact, taste and smell involve the assimilation of particles, possibly of only molecular dimensions, while sight and hearing have a wider range and enable us to observe objects at a distance by the radiations of light and sound which they emit. The last two faculties so far transcend the others in interest, though perhaps not in importance, that I shall confine myself to these and limit inquiry to the two questions—How do we see, and how do we hear?

*Annual Oration delivered to the Medical Society of London on May 8.

## Observation by Sight

We are enabled to see objects by the light which falls on them or is emitted by them. Light itself consists of groups of electro-magnetic waves which travel across space with almost inconceivable velocity, the waves themselves so small that from two thousand to four thousand would occupy only a millimetre. Where we see objects by illumination the waves are absorbed by the atoms of the object and then emitted by these atoms in a modified form. Let us examine these statements a little more closely.

Light is not the only kind of radiation with which we are acquainted. It forms, in fact, only one octave in the vast complex of vibrations with which space is filled. Some of these other vibrations we use, and through this room are passing hundreds of wave-groups radiating from transmitters, which we could detect through suitable receivers, from cosmic rays which arose somewhere in distant space to the programme of the B.B.C. All these are examples of electro-magnetic waves, and we are familiar with more than sixty octaves of such vibrations. But only one of these octaves constitutes light, and to this octave we are indebted for all that we see, whether we are reading the pages of a newspaper or watching a glorious sunset, or looking through a telescope at a distant star. Perhaps it is as well that for only this minute fraction of a vast complex have we any means of perception.

Let us, however, look for a moment at the origin of these waves of light, at the atoms from which they arise, and about whose characters they tell us. In the modern view each atom consists of a nucleus around which circulate a number of electrons. In its normal state the number of electrons is fixed for the atom of each element and is in fact the distinguishing characteristic of the element. Hydrogen has one electron, helium two (Fig. 1), lithium three, and so on up to uranium with 92. Moreover, the electrons revolve in orbits whose measurements are known with great accuracy.

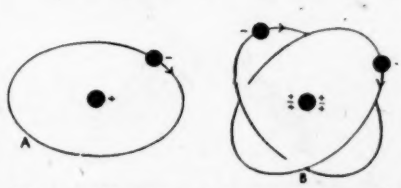



FIG. 1.—Hydrogen (A) and helium (B) atoms.

The orbits are not always the same, for if an atom absorbs energy it does so by the displacement of an electron to a wider orbit; when the electron returns to its normal

orbit the same energy is given out, perhaps as a group of waves of light. Moreover, the energy is absorbed or given out not in a continuous stream but in little packets of chains of waves termed photons. The absorption and emission of energy by an atom are thus the outward signs of the displacement of an electron from its orbit and of its return. The absorption and emission of light and energy are entirely the business of these electrons. If energy is absorbed certain electrons move to wider orbits, and when they drop back to their normal circuit the same energy is given out again.

It will be seen, then, that from the strictly physical aspect any observation depending on the use of light is an affair of extreme complexity, and though the observation may seem to us the simplest thing in the world it is in fact based on vast assumptions for the validity of which we can only cite our general experience. But what relation our observations bear to the profound reality which lies behind we have no means whatever of knowing, and it is quite certain that it would be utterly beyond our comprehension.

### Mechanism of Sight

Let us now turn to the other side of the picture and study the mechanism by which light makes an impression upon *us*—the means, in fact, by which we see. You are all familiar with the eye as an optical instrument in which an image is formed on the sensitive retina (Fig. 2). Developmentally the retina is an extension of the brain, and it consists of a vast forest of cells of two special forms—rods and cones—with the unique property of being sensitive to light. In each retina there are some seven million cones and 100 million rods, and although small groups may share one conducting fibre there are many million fibres, each with its own insulating sheath, in each optic nerve.

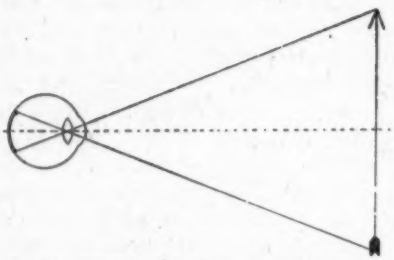


FIG. 2.—Path of light rays to the retina.

The optic nerves, carrying the whole of the light impulses from the two retinae, pass backwards to the optic chiasma, and here the nerve fibres which form the two nerves are redistributed in a very remarkable way. The fibres from the left-hand sides of both retinae join to form the left optic tract, while those from the right-hand sides of both retinae form the right optic tract (Fig. 3). The effect of this is that the whole of the right visual field is served by the left optic tract, while the left visual field is served by the right optic tract.

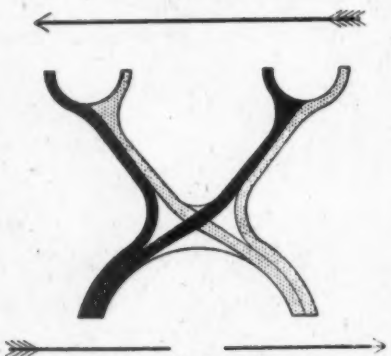


FIG. 3.—Optic chiasma.

The two optic tracts pass backwards beneath the brain to certain relay stations, from which they are again distributed. The true visual fibres are relayed by the optic radiations to the visual cortex of the two occipital lobes, where are situated the primary cortical centres for sight (Fig. 4). Other relays serve centres for eye movements, focusing, and the pupil reflex, all of which are essential to accurate vision. It will thus be realized that a large part of the light which enters the eyes is absorbed in the operation of a very elaborate mechanism of whose action we are almost completely unconscious, and that only a small portion is actually relayed to the visual cortex.

The visual cortex appears to present an exact point-to-point correspondence with the retina, so that one can regard the retinal image as actually transferred to the visual cortex, with, however, one very remarkable difference. On each retina the whole visual field is received, but each occipital lobe receives only the contralateral half of the field. Yet we are entirely unconscious of any such division, for the image has not yet reached a level in the brain at which it can be appreciated. From the visual cortex the image is transferred by well-marked tracts of fibres to many regions in the brain where it can take its share in many reflex activities. In the angular gyrus it adjoins the sensory cortex, where it makes contact with the sense of touch; and here the meaning of objects is recognized—the difference, for example, between a pencil and a penknife. Transference to the speech centre enables printed or written words to be recognized, and, further on in the motor centres, to be reproduced in speech or writing. Connexions with the auditory centre enable us to interpret the sound represented by printed words or music. Finally, a massive band of fibres conveys the image to the frontal lobes, the region probably of higher psychic analysis.

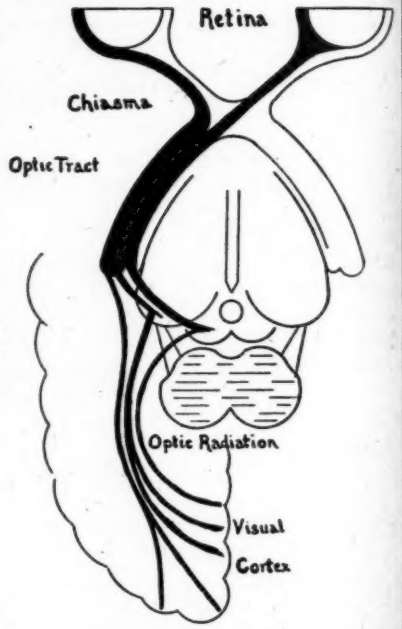



FIG. 4.—Diagram showing the visual paths.

It is clear, then, that the image focused by our eyes is distributed to almost every portion of the brain and that there it fuses with other impulses to form a whole series of collateral effects. In every region it is confronted with earlier memories, until the whole forms a complex utterly defying analysis. Yet of all this complicated process we are entirely unconscious, and its detail is brought to our notice only when some item fails. Some of you may suffer from migraine and are familiar with the dazzling fortification lines, followed perhaps by a complete blackout of one-half of the visual field. If so, you have had the opportunity of observing the effects of spasm of one of the arteries supplying the occipital lobe. It may console you that you have had definite proof that your arteries are still young and elastic.

When we look at a scene I suppose that most of us imagine that it is reproduced in our brain very much as it would be reproduced on the film of a camera, but what

actually happens is very different. The scene is in fact formed as an image on the retina of each eye, but these images are first split into left and right, then each pair combine on opposite sides of the brain, then these split images are re-combined and brought into relation with impulses from many other sources and filtered through a whole mass of memories. The final complex is what we see, and it is only after this infinity of preparation that the scene reaches our consciousness. Is it not amazing that what we see bears any relation at all to the facts and that on the whole the visual sensations of different individuals correspond so closely?

### Observation by Sound

Let us turn to another of the means by which we make contact with the outside world, our sense of sound. Like light, sound is propagated by waves, but of a very different nature—by means of compression and rarefaction of the air. The waves are produced by the vibration of solid objects, and if the sound is musical in character the waves must recur in regular periods, though they may be of any form. Upon the number of waves per second depends the pitch of the sound; upon the form of the wave depends its character — from the simple wave emitted by a tuning-fork to the complex wave of the oboe (Fig. 5).

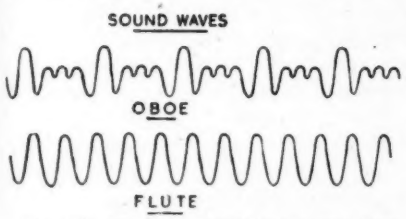


FIG. 5.—Sound waves of oboe and flute.

Sound waves have two remarkable properties. In the first place, they are capable of infinite variety, so that the most complex sound produced by a modern orchestra can be embodied in a succession of wave forms, and indeed it is only as such that it can affect our ears. But even more remarkable is the fact demonstrated by the great mathematician Fourier that these wave forms, however complex, can by a suitable analysis be reduced to a group of simple harmonic vibrations such as a tuning-fork emits. Moreover, this analysis, one of the great feats of mathematical skill, is carried out automatically by our ears, and it is the analysed wave, broken up into its constituent fractions, and not the crude wave of sound, which is transmitted to our brains. And apparently, so far as the mechanism of the ear is concerned, this analysis has nothing to do with musical appreciation, and indeed may be just as perfect in a cat as in a virtuoso.

The nerve impulses which arise from the sound, each representing a single term in the Fourier analysis, are conveyed to the brain by the auditory nerve, each apparently by a separate nerve fibre, and after suitable relays are conveyed to the temporal lobe on the opposite side of the brain. Just as the occipital lobes provide the receptive cortex for sight, so do the temporal lobes provide the receptive cortex for hearing, but this is still far from the level of consciousness. Numerous fibre tracts connect the auditory cortex with the other regions of the brain, with areas of touch, of sight, of motion. Thus without any actual involvement of consciousness we may turn to see whence a sound comes or spring aside to avoid danger. Beyond these areas, again, lies the level of consciousness where we can analyse the nervous impulses and compare them with our memories. It is here in the hidden recesses of the brain that the power of the musician lies, and almost certainly not in the actual mechanism of the ear itself.

Beethoven was stone deaf when he wrote the music of his last and greatest phase, and it is indeed to this that we owe his finest pianoforte sonatas, for no pianoforte then existed capable of producing their majestic power. It is said that when he conducted the first performance of the Choral Symphony the audience rose to their feet to applaud at the conclusion. But the conductor remained facing the orchestra, till the leading soprano came forward and took him by the hand to turn towards the audience the only man who had not heard a single note.

Musicians tell me that when they read the score of a symphony they hear the harmonies as clearly as if they were listening to an orchestra. With these fortunate people sound memories and the visual pictures of notes are so combined that the eye can almost replace the ear. To Beethoven the movement of the bows of the violins brought back the memory of his creation so vividly that I do not for one moment suppose that he realized his deafness and that no sound could penetrate his ears. His vast genius lived again in the world of its own inspiration.

### Composite Pictures

I have tried to show you something of the mechanism by which waves of light and of sound gain access to the brain and how they are distributed and fused with stimuli arising from other sources. So much is this the case that it would scarcely be an exaggeration to say that every region of the brain is affected by every stimulus which reaches the level of consciousness.

The interlocking of all the regions of the brain generally passes unnoticed, but occasionally some unusual effect calls for our attention. Many years ago on a holiday in the Black Forest I heard the Kreutzer Sonata being studied by two young musicians. Two years later I heard it again in Oxford, and with the great opening chord passage I was overwhelmed by the smell of pines. I was so astonished that it was some moments before I remembered my summer in the pine forest of Germany. You could scarcely have a more dramatic illustration of the diffusion of stimuli through the brain.

We have thus reached the conclusion that whenever we make any observation we build up in our brain a set of

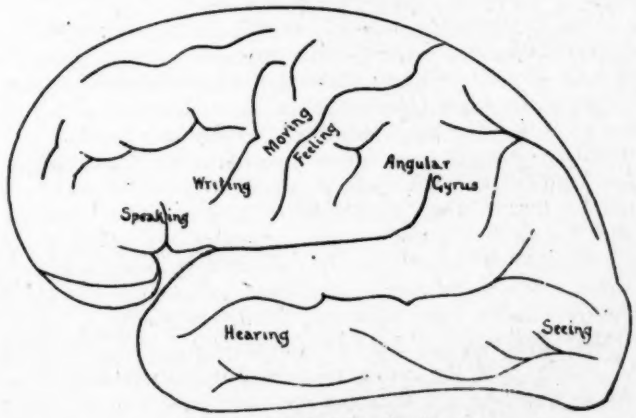


FIG. 6.—Cortical localization.

composite pictures in each of which are united groups of impulses which have entered the brain through different ports of entry. So far we are in the realm of ascertained fact, and we even know the region of the brain where these primary composite pictures are formed (Fig. 6). Moreover, the nerve stimuli which form these images are all identical in nature and differ only in the situation of the particular

cells affected. For example, in the region of the angular gyrus certain cells receive messages from the visual cortex, others from the sensory cortex, but all these messages, however varied their meaning, now give rise to cell activities identical in nature and differing only in position. And these activities, so different in origin, are here combined and passed to other cells for transmission to other regions of the brain.

The brain contains some ten thousand million nerve cells, and these are of many types and no doubt serve many special functions, but the point I wish to make is that so far as we can discover these cells transmit activity by similar processes and to them it is a matter of complete indifference whether the message entered initially by the eye, or the nose, or the ear.

But although we cannot follow the stimuli further into the anatomy of the brain we can appreciate other stages in analysis which may well have an anatomical basis. For example, one recognizes a square as a square, or a circle as a circle, whatever its position, and this is something beyond the capacity of the initial regions of combination such as the angular gyrus. But this capacity is very limited, as you may easily satisfy yourself by trying to read a book upside down. Possibly a higher development of such a faculty may explain the vagaries of the futurist.

### Memory, an Essential Basis

We have traced the passage of nerve impulses from their varied origin as far as we can penetrate into the dim regions of their final synthesis. The passage is accompanied by a by-product which is for us of vital importance. It is a fundamental law of all nerve activity and transmission that each occurrence facilitates the next similar occurrence. Why or how this happens we do not know, but it is a simple and recognized fact which indeed forms the physiological basis of our lives. You see it in perhaps its most perfect form in the musician who practises a simple figure until it becomes subconscious and automatic. On the more extended scale this facility, acquired by the recurrent passage of similar stimuli, is the basis of memory. Moreover, as I have shown you, a single stimulus from one source—for example, a sound or a smell—may arouse a whole complex of forgotten memories.

Now, memory has two sides. We can create memories by repetition, but we use those memories in the appreciation of fresh stimuli. Without these memories the world around us would be meaningless, for we should have no basis of comparison. It would be a book written in a language of which we did not even know the characters. Memory is the essential basis of observation. If this view is correct it follows that a baby has at birth no true power of observation, for it has none of the memories on which alone observation can be based. In one sense its brain is a clear tablet ready to receive impressions, although of course it possesses latent traits inherited through the ages.

We have reached the fundamental point which I wish to make, that the value of any observation is entirely conditioned by the mass of recorded observations which form the stock-in-trade of our personality. In an orderly brain these form a library of reference in which every new fact is filed. Most of our observations pass through along well-worn paths without raising a ripple, but every now and then one of them does not quite fit in and we look at it again. We may be on the brink of a great discovery. But notice that it is the content of the observer's brain, the slow accumulation of years of toil, that has made possible this moment of triumph.

### Comparison of Old and New Perceptions

I suppose that for countless aeons of time men watched the stars stream across the sky before one of these men noticed that one of the stars had moved from its place. But that man himself must have watched the stars for years till their permanent relation was fixed in his mind and he was startled to find that one had changed its place. You can imagine that he kept the secret to himself and watched night after night to see if it were really true. And if he were a wise man the more certain he became the more closely would he guard such a revolutionary discovery.

From this standpoint observation consists in the comparison of the new picture with the old. Agreement generally passes unnoticed or may give a certain sense of satisfaction. Disagreement induces a feeling of unrest and a desire for solution. But I believe that the matter goes deeper than this, and that such agreement is the physiological basis of pleasure. We all know the pleasure of familiar scenes, of well-known music. But here the basis of pleasure is too complex for analysis. The resolution of a chord or the fusion of two geometrical patterns are simpler examples, the complex in each case resolving into the simpler form. There is, however, one curious example where we can actually watch the comparison and ultimate fusion of two pictures in the brain—in stereoscopic vision. Here different but complementary pictures are presented to the two eyes and after a moment of confusion are fused in the brain, forming now one picture with the quality of solidity. The moment of fusion is accompanied by a feeling of satisfaction which may under certain circumstances have all the subtle qualities of pleasure.

In the modern view the brain consists of a vast number of neurones, varying in detailed structure but of the same general type, each capable of receiving impressions and of transmitting these, perhaps greatly reinforced and probably modified, to other and perhaps distant regions of the brain. I do not know which is the more astonishing—the simplicity of the neurone as a unit or the vast complexity of the combination of these simple units in the brain. Up to a certain point we can follow our observations through this forest, but they are lost long before they have reached their final goal and even before they have become apparent to our consciousness. So far we can follow their physiological course, but where and how do they reach *us*? That is for ever beyond our ken, but at a certain level in the brain the passage of nerve impulses affects our consciousness, and, moreover, at this level we have some power of controlling them. It is easy to see how at lower levels constant repetition may produce facility, but how is that repetition ordered and how is it controlled? That we shall never know.

### External Aids

You will see by now that the most trivial observation, far from being a simple process, involves mechanisms of unimaginable complexity. The mechanism of the outer world by which it makes itself known to us is complex enough, but this is simple when compared with the mechanism in our bodies by which we receive these impressions. Yet it is only through this strange and incomprehensible machine of our own that we make contact either with the outside world or with one another. Its proper use is of vital importance to our understanding, and is, of course, the aim of education. But, regarding it solely as a machine, can we improve its services? We can correct certain physical defects by such means as spectacles and auditory aids. We can extend its powers by the use of telescopes and microscopes, which indeed open up for us

new worlds. Although heaven has limited our vision to one octave of light waves, by cunning devices such as radar and wireless we can extend our observations over vast fields of space and time. In such ways we do indeed increase our powers of observation, but sometimes with rather disconcerting effects.

Powerful telescopes enable us to see into regions of space where all the physical conditions are utterly outside our experience, but few of us ever realize the strangeness of the world into which we peer. We can study the moon in quite minute detail, but can we really grasp the fact that we are looking at an arid desert devoid not only of water but of air, where the temperature is either far above boiling point or a hundred degrees below freezing? We look at Jupiter and think of the glory of its moons, but can we ever realize that its dead and frozen surface is for ever hidden from us by vast clouds of ammonia?

The new 200-inch reflector in California enables us to explore unimagined regions of space, and one of the first photographs taken with it was of a distant nebula. This nebula probably consists of millions of stars and may be as extensive as the whole of our own stellar system, but the point of interest is its distance and the time its light has taken to reach us—no less than a thousand million years. Now astronomers assert that the whole age of the stellar universe is certainly less than four times this period, and it is quite certain that when those rays of light started on their way our solar system did not exist. Moreover, the nebula we see to-day is the nebula of a thousand million years ago, and for all we can know it may long ago have vanished.

Or again, we look through a microscope and see the exquisite form and perfect arrangement of the cells of some tissue. Do we always quite grasp that we are looking at an artifact which has only a remote connexion with reality? The beautiful colour, the sharp outlines which delight us, we owe to the skill of the technician who made the preparation and to tissue reactions which have no connexion whatever with the life of the tissue as part of a living organism.

You will see, then, that these external aids, valuable though they are, carry with them certain illusions which we must appreciate if we are to use them to advantage. It is indeed a fatal mistake to accept as gospel all the technical detail with which science can furnish us without first correlating it with our own unaided observation and fusing it all into one coherent whole. This is true even of observation in the physical universe, but how much more is it so in the complex world of the human body?

### Internal Mechanism

We can indeed improve our observation by external means, but far transcending these in importance is the power we undoubtedly possess of improving our own internal mechanism by its exercise and by the storing of memories. For the physical basis of memory is only a path along which messages can flow more freely so that our observations move along well-worn channels with a minimum resistance and a maximum effect. But the mere casual accumulation of memories is not enough. They must be accurate, they must be connected, and they must be arranged in coherent groups. May I give you an example?

A physician is standing by a child's bedside; his fingers are on its wrist. He feels the dry hot skin. He notes the racing pulse and estimates its power, its quality, its regularity. He sees the flushed face with its tinge of blue; he sees the nose expanding at each quick intake; he hears the hurried respiration and characteristic grunt. And he knows that he is faced with a case of acute pneumonia with a certainty which nothing but direct clinical observation can afford. His long experience has gathered together a great number of separate impressions into one clear picture. He is a trained clinical observer, and all his impressions are grouped together subconsciously into one observation which sweeps away irrelevant detail and grasps the one essential fact.

If observation is of such importance can we by any means develop and improve it? As regards the primary organs of sensation—our touch corpuscles, our taste buds, our ears, our eyes—we have probably very little, if any, power of modifying them at all. But in the higher centres of reception and co-ordination we have very great powers of development. Touch can be developed to distinguish variations of thickness of a thousandth of an inch; the trained musician can perceive variations in pitch which most of us could not distinguish. We can, in fact, in every field develop our power of primary perception.

But of far greater importance is our immense capacity for developing the combination of primary perceptions, for, as I hope that I have shown you, every observation we make has two aspects. On the one hand its character and its value depend on a vast train of preceding observations reaching back to our earliest infancy. On the other hand it leaves behind an impress which will affect every fresh observation we make into the distant future. Every observation is actually a conditioned reflex. By our observations and our memories we really create new worlds for ourselves through which we can wander at our pleasure. The historian can live again in the past; the musician can explore the limitless world of sound, of balanced periods, and of subtle harmonies; the mathematician can explore all the vast fields of space and time—perhaps, like Newton, "for ever voyaging through undiscovered fields of space alone."

The world of observation is a wonderful world, limitless in its possibilities, absorbing in its vast opportunities. And yet if we are really to enter it and to enjoy it to the full we must carry with us a spirit that seems its very contradiction—the spirit of adventure, of freedom from the restraint imposed by experience, the happy irresponsible spirit of a child. For there is another world which we may well envy, which perhaps only a child can enjoy in all the wonder of freedom, untrammelled by the bounds of convention, limitless in its imagination, inhabited by strange and delightful monsters and by fairies who sweep away all difficulties with the wave of a magic wand. Is their world the real one, or is ours? Can we still believe in fairies?

---

The classification of hospital posts used by the Central Medical War Committee differs from that used by the Ministry of Health in its Terms and Conditions of Service of Hospital Medical Staff. The Ministry has therefore sent a circular to hospitals asking them to use dual descriptions in advertisements for the next few months. They are as follows:—House-officer posts: House officer—first post (A) (second or third post (B2), as the case may be); or house-physician (or surgeon, etc.), salary £350 (A), £400 or £450 (B2) a year according to experience. Registrar posts: Junior registrar (B1); registrar (B1); senior registrar (B1). Junior hospital medical officer (B1). The Ministry hopes that it will be possible to discontinue the old classification into A, B2, and B1 by September 30.

# INTERMITTENT DOSAGE IN THE TREATMENT OF PULMONARY TUBERCULOSIS WITH STREPTOMYCIN

## A REPORT TO THE STREPTOMYCIN IN TUBERCULOSIS COMMITTEE OF THE MEDICAL RESEARCH COUNCIL

BY

J. R. BIGNALL, M.A., M.D., M.R.C.P.*
J. W. CLEGG, M.R.C.S., D.C.P.
J. W. CROFTON, M.A., M.D., M.R.C.P.*
(*From the Institute of Diseases of the Chest and Brompton Hospital*)

B. J. DOUGLAS SMITH, M.B., B.S.
H. D. HOLT, M.R.C.S., D.P.H., Dipl.Bact.
(*From the Colindale Hospital*)

D. A. MITCHISON, B.A., M.B., B.Chir.
(*From the Postgraduate Medical School of London*)

AND

P. ARMITAGE, B.A.
(*From the Medical Research Council's Statistical Research Unit, London School of Hygiene and Tropical Medicine*)

The emergence of drug-resistant tubercle bacilli has been the major difficulty in the streptomycin treatment of pulmonary tuberculosis. In the first Medical Research Council series of cases of pulmonary tuberculosis treated in this country (Medical Research Council, 1948a) strains showing a streptomycin resistance more than 10 times that of the control were isolated from 35 out of 41 cases. The resistant organisms were usually first found within two months of beginning treatment, occasionally later. Towards the end of 1947, when the first trial was finishing, it was already obvious that any way of avoiding or delaying the emergence of resistance would be a major advance.

The quantitative studies of Pyle (1947) had shown that in pulmonary tuberculosis a minute proportion of streptomycin-resistant tubercle bacilli could be isolated from large inocula of the apparently sensitive pre-treatment strain. As streptomycin treatment continued and the sensitive organisms were gradually eliminated, the resistant minority came to occupy a larger and larger proportion of the bacterial population. Eventually the proportion was sufficient to manifest streptomycin resistance in the comparatively crude routine tests. It seemed, therefore, that even in the absence of streptomycin there was a steady but very low mutation rate to streptomycin-resistant forms. In spite of this steady mutation the proportion of resistant forms did not seem to increase unless they were put at an advantage by exposure to the drug. This failure to increase suggested that in the absence of streptomycin the resistant bacilli might be at a disadvantage, and might therefore tend to die out during intermissions in treatment.

It was known, of course, that once resistant forms were demonstrable in the crude tests it was unusual, in the individual case, to get reversion to sensitive strains. But it was unlikely that a single injection of streptomycin would eventually result in an entirely resistant bacterial population. Somewhere between these extremes the process might be reversible. It appeared possible, therefore, that by a suitable intermission of dosage the process of resistance development might be retarded, or even prevented, without loss of clinical effect.

It was accordingly decided to try out the following rhythms of dosage.

*Group 1.*—Alternate weeks group : 0.5 g. of streptomycin six-hourly in alternate weeks.

*Group 2.*—Alternate months group : 0.5 g. of streptomycin six-hourly in alternate months (the month being a four-weeks period).

*Group 3.*—Control group : 0.25 g. of streptomycin six-hourly without intermission.

*Group 4.*—Single-dose group : 1 g. of streptomycin in one dose daily without intermission.

The above regimes were to be continued over a total period of six months (168 days), at which time all cases would have had the same total dose of streptomycin. The time of emergence of streptomycin resistance, as judged by the crude routine test, was to be assessed for each case and the results in the individual groups compared. It was hoped that in at least one of the trial groups there might be a significant delay in the emergence of resistance.

### Methods

The figures from the Brompton Hospital cases in the first Medical Research Council series (1948a) were used as a basis on which to judge the probable scatter of results. It was calculated that an average delay of a month in the emergence of streptomycin-resistant strains could be satisfactorily demonstrated if four cases were included in each treatment group. But it was decided that it would be wiser to aim at eight cases at least in each group, as it seemed possible that some might become sputum-negative or die before they had had six months' treatment or before resistant strains had been recovered.

As in the first Medical Research Council series the cases admitted to the trial were defined as follows : acute, progressive, bilateral pulmonary tuberculosis of presumably recent origin, unsuitable for collapse therapy : age group 15 to 30 years. In addition, cases were admitted only if there was a reasonable presumption, on account of cavitation or a strongly positive sputum, that the sputum would continue to be positive over a number of months. Cases which seemed unlikely to survive the treatment course were excluded. The trial was carried out at Brompton and Colindale Hospitals, and the same mechanism as in the first Medical Research Council series was used for recruiting and selecting cases and for allotting them at random to the different treatment groups. Each case was observed in hospital for at least a week before treatment was started, and during this time at least two sputa were cultured. After this, sputum was usually cultured once a week and tests for streptomycin sensitivity were performed as previously described (Medical Research Council, 1948b). Formal clinical and radiological examinations were carried out once a month.

In analysing the results, any strain of tubercle bacilli showing a degree of streptomycin resistance eight times or more that of the control strain (H37Rv) is recorded as having developed some degree of streptomycin resistance, since these readings are outside the range of error of the method (Mitchison, 1949). The "mean day of resistance development" has been defined as the mean day between the day of streptomycin treatment on which the last sensitive strain was isolated and that of the isolation of the first of two successive resistant strains. The criterion of two

*Part-time members of the Tuberculosis Research Unit, Medical Research Council.

successive strains was adopted because in a few cases isolated resistant cultures were followed by a series of sensitive ones before the strains became constantly resistant. It was felt that it would be misleading to time the emergence of resistance on such isolated cultures. In case it might be argued that strains of comparatively low streptomycin resistance were unimportant clinically, an analysis was also carried out on the same lines, but organisms were regarded as resistant only if they were at least 64 times more so than the control strain.

Clinical progress has been assessed on data not involving the judgment of the observer—that is, weight, pyrexia, and sedimentation rate. Radiological evidence involves judgment; to avoid personal bias the assessment was made by a radiologist (Dr. L. G. Blair) who was otherwise unconnected with the trial.

## Results

*Material.*—Altogether 45 cases were admitted to the trial, the first in December, 1947. These were allotted as follows: Group 1, alternate weeks group, 9 cases; Group 2, alternate months group, 13 cases; Group 3, control group, 12 cases; Group 4, single-dose group, 11 cases.

In Tables IA and IB a comparison is made, for the different treatment groups, of the time taken for streptomycin resistance to emerge. If the criterion of streptomycin resistance is that two successive cultures have yielded tubercle bacilli of resistance at least eight times that of the control, there is no statistically significant difference between the groups (Table IA). The same is true if the criterion is taken as two cultures of resistance at least 64 times the control (Table IB). Nor is there any striking difference in the number of cases from which no resistant strains were isolated, though here, of course, the numbers are too small for any but a gross difference to emerge. Defining the maximum degree of resistance attained in each case as the highest degree of streptomycin resistance found in two successive cultures, there is also no gross difference between the groups (Table II).

TABLE IA.—*Differences Between Treatment Groups in the "Mean Day of Emergence" of Two Consecutive Strains with Streptomycin Resistance Greater than Four Times that of H37Rv*

| Treatment Group | Total Cases | Deaths | Streptomycin Resistance Remained Less than 8 Times that of H37Rv until Sputum-negative | "Mean Day of Emergence" of 2 Consecutive Strains of Resistance greater than 4 Times that of H37Rv | | |
|---|---|---|---|---|---|---|
| | | | | 0–69 | 70–149 | >149 |
| Group 1 .. | 9 | 0 | 0 | 4 | 4 | 1 |
| Group 2 .. | 13 | 1 | 2 | 5 | 5 | 0 |
| Group 3 .. | 12 | 0 | 2 | 4 | 4 | 2 |
| Group 4 .. | 11 | 0 | 1 | 3 | 5 | 2 |
| All groups | 45 | 1 | 5 | 16 | 18 | 5 |

The "mean day of emergence" is defined as the mean day between the day of streptomycin treatment on which the last sensitive strain was isolated and that of the isolation of the first of two successive resistant strains.

TABLE IB.—*Differences Between Treatment Groups in the "Mean Day of Emergence" of Two Consecutive Strains with Streptomycin Resistance Greater than 32 Times that of H37Rv*

| Treatment Group | Total Cases | Deaths | Streptomycin Resistance Remained Less than 64 Times that of H37Rv until Sputum-negative | "Mean Day of Emergence" of 2 Consecutive Strains of Resistance greater than 32 Times that of H37Rv | | |
|---|---|---|---|---|---|---|
| | | | | 0–69 | 70–149 | >149 |
| Group 1 .. | 9 | 0 | 1 | 2 | 3 | 3 |
| Group 2 .. | 13 | 1 | 3 | 2 | 2 | 5 |
| Group 3 .. | 12 | 0 | 3 | 4 | 1 | 4 |
| Group 4 .. | 11 | 0 | 1 | 3 | 1 | 6 |
| All groups | 45 | 1 | 8 | 11 | 7 | 18 |

TABLE II.—*The Differences Between Treatment Groups in the Degree of Streptomycin Resistance Reached by Two Consecutive Strains in Patients whose Sputum Remained Positive Throughout 24 Weeks' Treatment*

| Treatment Group | Total Cases | Deaths | Sputum-negative Before 168th Day | Degree of Resistance in Multiples of that of H37Rv | | | |
|---|---|---|---|---|---|---|---|
| | | | | <8 | 8–32 | 64–512 | >512 |
| Group 1 .. | 9 | 0 | 1 | 1 | 2 | 3 | 2 |
| Group 2 .. | 13 | 1 | 3 | 0 | 5 | 3 | 1 |
| Group 3 .. | 12 | 0 | 4 | 2 | 2 | 1 | 3 |
| Group 4 .. | 11 | 0 | 1 | 2 | 4 | 1 | 3 |
| All groups | 45 | 1 | 9 | 5 | 13 | 8 | 9 |

It is clear that the trial has been unsuccessful in its primary object. No delay of the emergence of streptomycin resistance has been attained by any of the regimes tested. But in the course of treatment other results of interest have been reported and some of these will now be examined.

## Clinical Aspects

Analysis of the clinical results showed no important differences between the treatment groups, though of course the numbers were too small for any but gross differences to emerge.

Table III summarizes the extent of radiographic change after six months' observation. Analysis of the groups with regard to change in temperature, weight, and erythrocyte sedimentation rate at various stages of treatment also showed no important differences. It seems, therefore, that from the clinical point of view there is nothing to be gained by giving streptomycin in alternate weeks or months. In fact, we thought that very ill patients sometimes deteriorated in the periods off treatment, though this was not often clear-cut. The single injection a day, as opposed to six-hourly injections, is of course preferred by the patient; it seems to have no disadvantages, and is now generally adopted. In this connexion it should be added that in one case on alternate-months treatment resistant bacilli were first detected when the patient was in a rest period. A strain of resistance 32 times that of the control was isolated 20 days after the completion of the first month's streptomycin, two sensitive cultures having been previously obtained since stopping treatment.

TABLE III.—*Differences Between Treatment Groups in the Radiographic Change after 24 Weeks' Treatment*

| Treatment Group | Total Cases | Radiographic Change after 24 Weeks | | |
|---|---|---|---|---|
| | | No Improvement | Slight Improvement | Considerable Improvement |
| Group 1 .. | 9 | 3 | 1 | 5 |
| Group 2 .. | 12* | 2 | 6 | 4 |
| Group 3 .. | 11† | 2 | 4 | 5 |
| Group 4 .. | 11 | 1 | 3 | 7 |
| All groups | 43 | 8 | 14 | 21 |

* Excluding one patient who died before the 24th week. † Excluding one patient in whom the data were incomplete.

## Other Possible Factors Affecting Streptomycin Resistance

Since there were no significant differences between the four treatment groups in the time of emergence of streptomycin resistance or in its degree, it was of interest to see whether any correlation with other factors could be found. The factors examined were:

1. Condition before treatment, as assessed by (*a*) average evening temperature in the week before starting treatment; (*b*) erythrocyte sedimentation rate before treatment; and (*c*) degree of (i) cavitation and (ii) "confluence of shadows" in the radiograph before treatment; cases were classified in one of three categories.

2. Progress in the first two months and the first four months of treatment as assessed by weight change, temperature, sedimentation rate, and radiographic appearance.

Although a significant correlation could be demonstrated only between degree of confluence of radiographic shadows and time of emergence of resistance (Table IV), all the factors examined showed a slight trend in the same direction. There was a slight tendency for highly resistant strains to be found in patients who, by the above criteria, were most ill before treatment started, and for strains of low resistance to be found in those least ill. In the most-ill patients streptomycin-resistant strains were often isolated early; in the least-ill patients they tended to be isolated later. There was a tendency for highly resistant bacilli to be isolated from the patients who had responded least satisfactorily to streptomycin, the tendency being apparent after both two months' and four months' treatment.

TABLE IV.—*The Relationship Between the Degree of Confluence of the Shadows in the Pre-treatment Radiograph of 39 Cases and the "Mean Day of Emergence" of Two Consecutive Strains of Streptomycin Resistance Greater than Four Times that of H37Rv. Six Cases are Excluded—One Died and Five became Sputum-negative before Producing Resistant Strains*

| Degree of Confluence of Shadows in Pre-treatment Radiograph | Total Cases | "Mean Day of Emergence" of 2 Consecutive Strains of Streptomycin Resistance Greater than 4 Times that of H37Rv | |
|---|---|---|---|
| | | 0–69 | >70 |
| Slight .. .. .. | 12 | 2 | 10 |
| Moderate .. .. | 19 | 9 | 10 |
| Gross .. .. .. | 8 | 5 | 3 |
| Total .. | 39 | 16 | 23 |

Analysis of these figures for trend towards delay of resistance emergence with diminishing confluence gives $\chi_1^2 = 4{\cdot}17$, $P < 0{\cdot}05$.

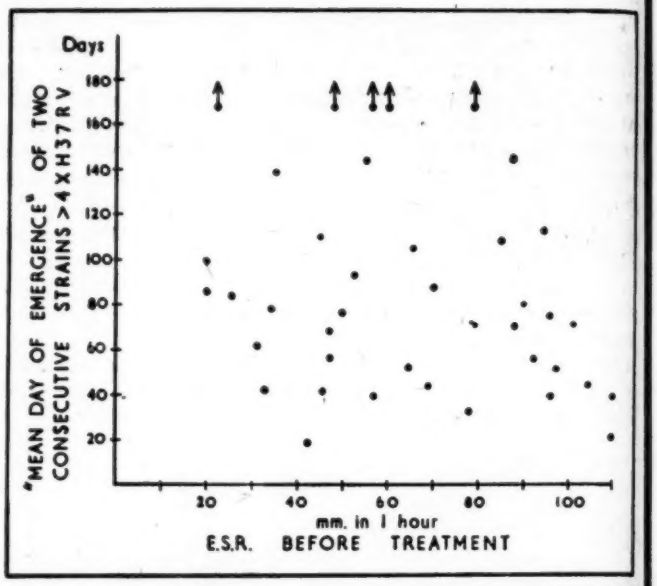



FIG. 1.—The relation of pre-treatment erythrocyte sedimentation rate to the "mean day of emergence" of two successive strains of streptomycin resistance greater than four times that of H37Rv. The arrows indicate the cases from which no streptomycin-resistant tubercle bacilli had been isolated at the end of 24 weeks' observation. The only apparent relation is in the highest and lowest ranges of sedimentation rate.

Strains of relatively low resistance were more likely to be isolated from patients who had responded well to the drug. Here, again, strains of high resistance often emerged relatively early and those of low resistance relatively late. As an example of these slight trends, Fig. 1 indicates the relation between pre-treatment erythrocyte sedimentation rate and the time of emergence of streptomycin resistance. The correlation was no more impressive for the other factors mentioned, and there were often gross deviations from the slight general trend, especially in the middle range.

As might be expected from the above analysis, there was a statistically significant correlation (Table V, Fig. 2) between the maximum degree of streptomycin resistance in the bacilli of a given case and the time at which resistant strains were first detected. This result might have been due to strains of low resistance emerging late and not having time to develop high degrees of resistance before the end of six months. But in a number of cases with low-resistance strains treatment was intentionally continued for eight months and no important further rise in resistance occurred.

TABLE V.—*The Relationship of the "Mean Day of Emergence" of Two Consecutive Strains of Streptomycin Resistance Greater than Four Times that of H37Rv and the Degree of Resistance Reached by Two Consecutive Strains in Patients whose Sputum Remained Positive Throughout 24 Weeks of Treatment*

| "Mean Day of Emergence" of 2 Consecutive Strains of Resistance Greater than 4 Times that of H37Rv | Total Cases | Degree of Resistance in Multiples of that of H37Rv | | |
|---|---|---|---|---|
| | | 0–8 | 16–512 | >512 |
| 0–69 days .. .. .. .. | 15 | 3 | 5 | 7 |
| >69 days .. .. .. .. | 20 | 14 | 4 | 2 |
| Total .. .. | 35 | 17 | 9 | 9 |

$\chi_2^2 = 9{\cdot}47$, $P < 0{\cdot}01$.

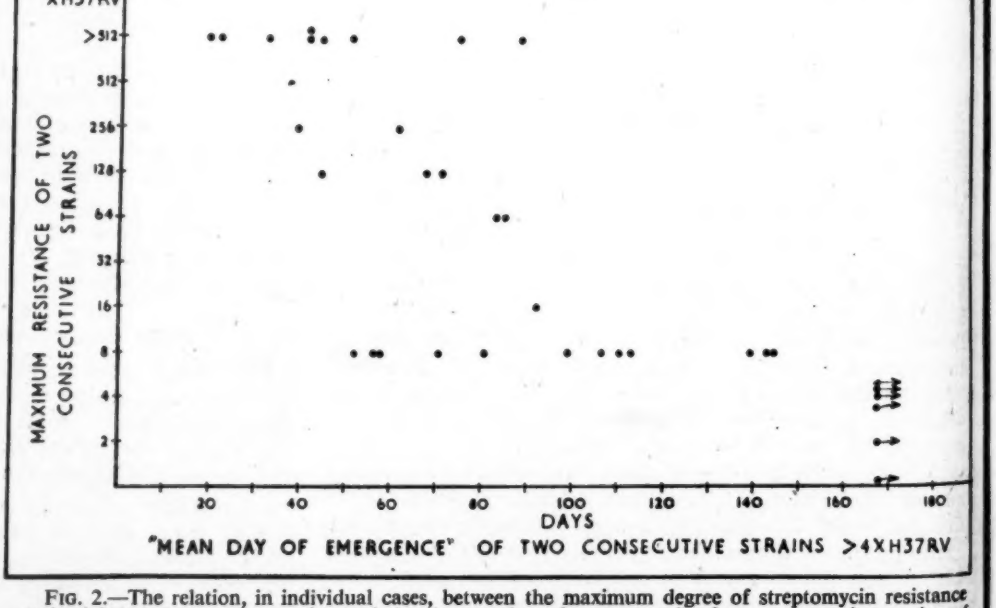



FIG. 2.—The relation, in individual cases, between the maximum degree of streptomycin resistance attained by two successive strains and the "mean day of emergence" of two consecutive strains of resistance greater than four times that of H37Rv.

### Sputum Examinations and Streptomycin Resistance

An attempt was made to see whether routine examination of the sputum could give any information about the progress of the case and the development of streptomycin resistance—apart, of course, from the obvious implications of consistent sputum conversion. The degree of positivity of each specimen for tubercle bacilli was graded as (1) direct smear strongly positive, (2) direct smear weakly positive, (3) direct smear negative, positive on culture only, or (4) negative on culture. Specimens were usually examined once a week.

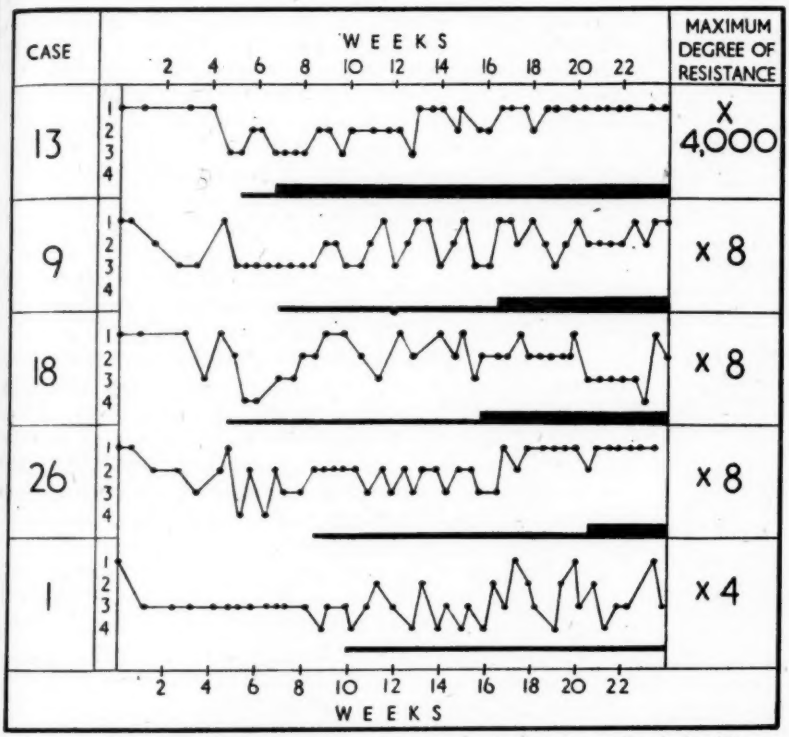



FIG. 3.—Relation of the emergence of streptomycin-resistant tubercle bacilli to the degree of positivity of the sputum. The vertical scale on the left indicates the degree of sputum positivity: (1) direct smear strongly positive; (2) direct smear weakly positive; (3) direct smear negative, positive on culture only; (4) negative on culture. The blocks indicate the time at which strains of tubercle bacilli emerged which were four times (lower blocks) or at least eight times (higher blocks) more resistant to streptomycin than the control strain (H37Rv).

In most cases (Fig. 3) there was a fall in the sputum positivity in the early stages of streptomycin treatment. When this fall was absent or minimal there was a strong tendency to develop a high degree of streptomycin resistance. There were 11 cases in which the direct smear was never found negative on three successive occasions. From all except one of these cases were isolated strains of resistance at least 128 times that of the control. In the exception (Fig. 3, Case 26) there appeared to be a fall in positivity, though in fact three successive negative smears were not obtained. But the reverse did not hold: three successive negative smears were obtained from six other cases from which were isolated strains of resistance at least 128 times that of the control.

After the initial fall in the positivity of the sputum there was usually a later rise (Fig. 3) unless permanent sputum conversion had been achieved. It could in general be said that when a persistent rise in sputum positivity occurred after the initial fall streptomycin-resistant strains would be detected on the routine test. This might be of some use to the clinician, as at present the routine test takes eight weeks. But there is an important proviso: this rise might occur whether the degree of streptomycin resistance was very high or relatively low.

There was often a rise in the sputum positivity after the consistent isolation of strains of a low degree of streptomycin resistance; even as low as four times that of the control, which is just within the limits of experimental error (Fig. 3, Cases 1, 9, 18, and 26). This strongly suggests that slight increases are of some clinical importance. But it seems that such slight increases are less important than great increases. In nine cases, none of which had had collapse therapy, the sputum culture remained negative for at least four weeks. In five of those no increase in resistance was detected; in one the maximum degree of resistance was four times the control, and in the remaining three eight times: this in spite of the fact that in seven out of the nine cases positive cultures were obtained more than 100 days after starting treatment, so that there had been plenty of time for highly resistant forms to emerge. It seems, therefore, that sputum conversion is more likely in cases in which bacilli show only a low degree of streptomycin resistance.

### Comparison with the First M.R.C. Series

One of the surprising results of the present trial is the smaller proportion of cases which developed high degrees of streptomycin resistance as compared with the first Medical Research Council series, in which the cases were treated with 0.5 g. of streptomycin six-hourly. The criteria for selection of cases were almost the same in each series. A comparison between the results from the present series and from the 24 cases of the first series treated at Brompton and Colindale Hospitals is given in Table VI. As in the cases of the first series streptomycin was usually stopped at four months, the comparison is made at 120 days after starting treatment. It will be seen that the differences between the two series are statistically significant. Whether this difference is due to the different dosage in the present series or to some other factor is uncertain.

TABLE VI.—*Comparison of the Maximum Degree of Streptomycin Resistance of a Single Strain Isolated During the First 120 Days of Treatment from the Group Treated at Brompton and Colindale Hospitals During the First M.R.C. Investigation and from the Intermittent Dosage Series. Those in whom the Sputum became Negative Before the 120th Day have been Excluded*

| Degree of Resistance in Multiples of that of H37Rv | Total Cases | First M.R.C. Series | Intermittent Dosage Series |
|---|---|---|---|
| <32 .. .. .. | 27 | 4 | 23 |
| >16 .. .. .. | 36 | 17 | 19 |
| Total .. | 63 | 21 | 42 |

$\chi^2 = 6{\cdot}05$, $P < 0{\cdot}02$.

Tables VII and VIII compare the condition before treatment in the two series. There is little difference except that the average pre-treatment temperature was a little higher in the first series. At two months and four months after starting streptomycin the cases in the present series fared significantly better as regards weight gain, pyrexia, and sedimentation rate (Tables IX, X, and XI). There are possible explanations for some of these findings. Cases in

TABLE VII.—*Temperature and Sedimentation Rate Before Treatment in the Group Treated at Brompton and Colindale Hospitals During the First M.R.C. Investigation and the Four Treatment Groups of the Intermittent Dosage Series. The "Mean Temperature" is the Mean Evening Temperature During the Week before Streptomycin Treatment was Begun*

| Treatment Group | Total Cases | Condition Before Treatment | |
|---|---|---|---|
| | | Mean Temperature °F. | Mean E.S.R. mm. in 1 Hour |
| | | S.E. | S.E. |
| First M.R.C. series: 0·5 g. 6-hourly continuously .. .. | 24 | 100·03 ± 0·28 | 57·75 ± 5·51 |
| Group 1 .. .. | 9 | 99·94 ± 0·45 | 58·33 ± 9·00 |
| Group 2 .. .. | 13 | 99·64 ± 0·30 | 71·54 ± 7·49 |
| Group 3 .. .. | 12 | 99·50 ± 0·22 | 63·92 ± 7·79 |
| Group 4 .. .. | 11 | 99·24 ± 0·26 | 61·91 ± 8·14 |

S.E. = Standard error.

TABLE VIII.—*The Radiographic Appearances Before Treatment in the Groups Treated at Brompton and Colindale Hospitals and the Four Treatment Groups of the Intermittent Dosage Series*

| Treatment Group | Total Cases | Radiographic Appearances | | | | | |
|---|---|---|---|---|---|---|---|
| | | Cavitation | | | Confluence of Shadows | | |
| | | Slight | Moderate | Gross | Slight | Moderate | Gross |
| First M.R.C. series: 0·5 g. 6-hourly continuously .. | 24 | 10 | 8 | 6 | 7 | 9 | 8 |
| Group 1 .. .. | 9 | 5 | 1 | 3 | 4 | 3 | 2 |
| Group 2 .. .. | 13 | 4 | 7 | 2 | 2 | 9 | 2 |
| Group 3 .. .. | 12 | 2 | 5 | 5 | 5 | 3 | 4 |
| Group 4 .. .. | 11 | 4 | 6 | 1 | 4 | 5 | 2 |
| Total .. | 69 | 25 | 27 | 17 | 22 | 29 | 18 |

the present series on 2 g. of streptomycin a day tended to gain weight more slowly than those on lower dosage, so that the higher dosage in the first series might have resulted in less gain.

The less satisfactory progress of the first series at four months, as regards weight gain, pyrexia, and sedimentation rate, might of course have been due to more cases having developed organisms with high degrees of streptomycin resistance. This argument is less applicable at two months, when in many cases resistant organisms had not yet emerged. We cannot say whether the first series did less well in these respects, because at two months the proportion of highly resistant tubercle bacilli was already increasing, or whether the highly resistant forms emerged because the patients had done less well. It is possible that neither is correct and that the differences in weight gain, pyrexia, and sedimentation rate were merely due to the more toxic effect of the higher dosage of streptomycin. It will be noted that as regards radiographic improvement the first series did rather better (Tables XII and XIII).

At four months the cases in the first series had had twice as much streptomycin as those in the present series. But if the figures for the present series are taken at six months there is still a big difference in the incidence of highly resistant organisms. At six months bacilli of resistance less than 32 times that of the control strain were grown from 14 out of 35 cases of the present series, compared with 4 out of 21 of the first series taken at four months. (These differences, though suggestive, are not statistically significant : $\chi^2 = 1.78$, $P = 0.2—0.1$). Again, daily dosage

TABLE IX.—*The Differences in the Temperature Change During the First Eight Weeks and the Second Eight Weeks Between the Group Treated at Brompton and Colindale Hospitals During the First M.R.C. Investigation and the Four Treatment Groups of the Intermittent Dosage Series. The Figure for Temperature is Based on the Mean Evening Temperature for the Preceding Week. The Figures in Heavy Type are Significantly Different from the Corresponding Figures for the Other Groups*

| Treatment Group | Temperature Change Degrees F. | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | After 8 Weeks | | | | From 8 to 16 Weeks | | | |
| | Total Cases | Mean Change | Mean Pre-treatment Temperature | Mean Change Allowing for Pre-treatment Differences | Total Cases | Mean Change | Mean Temperature at 8 Weeks | Mean Change Allowing for Differences at 8 Weeks |
| | | | | S.E. | | | | S.E. |
| First M.R.C. series: 0·5 g. 6-hourly continuously .. | 24 | −0·87 | 100·03 | **−0·86 ± 0·13** | 24 | −0·13 | 99·16 | **−0·02 ± 0·10** |
| Group 1 .. .. .. | 9 | −1·33 | 99·94 | −1·18 ± 0·22 | 9 | −0·14 | 98·61 | −0·21 ± 0·16 |
| Group 2 .. .. .. | 12* | −0·95 | 99·52 | −1·07 ± 0·19 | 12* | −0·21 | 98·58 | −0·29 ± 0·14 |
| Group 3 .. .. .. | 12 | −0·98 | 99·50 | −1·11 ± 0·19 | 12 | −0·27 | 98·52 | −0·37 ± 0·14 |
| Group 4 .. .. .. | 11 | −0·40 | 99·24 | −0·71 ± 0·20 | 11 | −0·45 | 98·84 | −0·44 ± 0·14 |

* Excludes one patient who died after four weeks' treatment.

*Note.*—The second column shows, for each group, the mean temperature change between 0 and 2 months after treatment. Since this change is correlated with the pre-treatment temperature (the largest fall being expected when the pre-treatment temperature is highest), it is desirable to know whether any differences there may be between the groups in mean change could be due merely to initial differences in pre-treatment temperature. The mean values of the pre-treatment temperature are shown in the third column. The fourth column shows the mean changes which would have been expected had there been no differences between the groups in mean pre-treatment temperature. The significance of differences between these corrected means has been assessed by the analysis of co-variance.

TABLE X.—*The Differences in the Change in E.S.R. During the First Eight Weeks and the Second Eight Weeks Between the Group Treated at Brompton and Colindale Hospitals During the First M.R.C. Investigation and the Four Treatment Groups of the Intermittent Dosage Series. The Figures in Heavy Type are Significantly Different from the Corresponding Figures for the Other Groups, Analysed as in Table IX*

| Treatment Group | Change in E.S.R. mm. in 1 Hour | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | After 8 Weeks | | | | From 8 to 16 Weeks | | | |
| | Total Cases | Mean Change | Mean Pre-treatment E.S.R. | Mean Change Allowing for Pre-treatment Differences | Total Cases | Mean Change | Mean E.S.R. at 8 Weeks | Mean Change Allowing for Differences at 8 Weeks |
| | | | | S.E. | | | | S.E. |
| First M.R.C. series: 0·5 g. 6-hourly continuously .. | 24 | −2·21 | 57·75 | **−3·54 ± 4·71** | 23† | −12·09 | 54·91 | **−10·51 ± 4·03** |
| Group 1 .. .. .. | 9 | −10·67 | 58·33 | −11·81 ± 7·67 | 9 | −18·67 | 47·67 | −19·54 ± 6·41 |
| Group 2 .. .. .. | 12* | −14·92 | 70·00 | −12·16 ± 6·69 | 12* | −16·58 | 55·08 | −14·95 ± 5·55 |
| Group 3 .. .. .. | 12 | −17·85 | 63·92 | −17·03 ± 6·64 | 12 | −17·00 | 46·08 | −18·41 ± 5·55 |
| Group 4 .. .. .. | 11 | −20·00 | 61·91 | −19·95 ± 6·93 | 11 | −13·00 | 41·91 | −15·83 ± 5·79 |

* Excluding one patient who died after four weeks. † Excluding one patient in whom the data were incomplete.

TABLE XI.—*The Difference in Weight Change During the First Eight Weeks and the Second Eight Weeks Between the Groups Treated at Brompton and Colindale Hospitals During the First M.R.C. Investigation and the Four Treatment Groups of the Intermittent Dosage Series*

| Treatment Group | Weight Change (lb.) | | | |
|---|---|---|---|---|
| | After 8 Weeks | | From 8 to 16 Weeks | |
| | Cases | Mean Change | Cases | Mean Change |
| First M.R.C. series: 0·5 g. 6-hourly continuously .. | 20* | +1·40±1·16 | 19‡ | +0·63±1·08 |
| Group 1 .. .. | 9 | +4·00±1·73 | 9 | +5·11±1·57 |
| Group 2 .. .. | 12† | +4·16±1·50 | 12† | +3·41±1·36 |
| Group 3 .. .. | 12 | +6·58±1·50 | 12 | +5·83±1·36 |
| Group 4 .. .. | 11 | +6·45±1·57 | 11 | +6·55±1·42 |

* Excluding 4 patients in whom the data were incomplete; in 3 because they were too ill to weigh. † Excluding one patient who died after 4 weeks. ‡ Excluding 5 patients in whom the data were incomplete; in 4 because they were too ill to weigh.

alone cannot explain the discrepancy, for of those positive at four months 10 out of 20 cases in the present series receiving 2 g. a day by intermittent dosage showed strains of resistance under 32 times that of the control, compared with 4 out of 21 in the first series. (The differences are almost, but not quite, statistically significant : $\chi^2 = 3.15$, $P = 0.1—0.05$.)

To sum up : it is unlikely to be fortuitous that a smaller proportion of the present series developed high degrees of streptomycin resistance as compared with the first Medical Research Council series. The reason for this we have been unable to determine. It may be that there were important differences which we were unable to detect in the composition of the two series. It may be the fact that, over two or four months, the present series received only half the quantity of streptomycin, or that the dosage was differently spaced. The apparent differences in the response to treatment may provide a clue. Or there may have been some other factor which we failed to assess.

TABLE XII.—*The Difference in Radiographic Change after Eight Weeks Between the Group Treated at Brompton and Colindale Hospitals During the First M.R.C. Investigation and the Intermittent Dosage Series*

| Treatment Group | Total Cases | Radiographic Change | |
|---|---|---|---|
| | | Improved | Not Improved |
| Group 1 .. .. | 9 | 3 | 6 |
| Group 2 .. .. | 11* | 3 | 8 |
| Group 3 .. .. | 12 | 5 | 7 |
| Group 4 .. .. | 11 | 3 | 8 |
| Groups 1–4 .. .. | 43 | 14 | 29 |
| First M.R.C. series: 0·5 g. 6-hourly continuously .. .. | 24 | 11 | 13 |

* Excluding two patients in whom the data were not available.
Comparing the two series, $\chi^2_1 = 1·16$, P = 0·2–0·3: this difference is not significant.

TABLE XIII.—*The Differences in Radiographic Change after 16 Weeks' Treatment Between the Group Treated at Brompton and Colindale Hospitals During the First M.R.C. Investigation and the Intermittent Dosage Series*

| Treatment Group | Total Cases | Radiographic Change | |
|---|---|---|---|
| | | Improved | Not Improved |
| Group 1 .. .. | 9 | 8 | 1 |
| Group 2 .. .. | 12* | 9 | 3 |
| Group 3 .. .. | 12 | 9 | 3 |
| Group 4 .. .. | 11 | 10 | 1 |
| Groups 1–4 .. .. | 44 | 36 | 8 |
| First M.R.C. series: 0·5 g. 6-hourly continuously .. .. | 23† | 17 | 6 |

* Excluding one patient who died after four weeks. † Excluding one patient in whom the data were incomplete.
Comparing the two series, $\chi^2_1 = 0·57$, P = 0·3–0·5 : this difference is not significant.

## Discussion

It is disappointing that intermittent dosage as used in this trial has been quite ineffective in avoiding or delaying the emergence of drug-resistant strains of tubercle bacilli. This suggests that the process of replacement of a streptomycin-sensitive bacterial population by streptomycin-resistant forms continues, at least to some extent, during intermissions in treatment. This conclusion is supported by the findings in one case on alternate-months treatment, in which a resistant culture was first obtained in a rest period 20 days after completing the first month's treatment.

Jensen's (1949) experiments and some unpublished investigations by one of us (J. W. Clegg) suggest that small quantities of streptomycin may persist in the body for a number of weeks after stopping treatment. The tubercle bacilli may therefore continue for some time to be exposed to low concentrations of the drug. Possibly some other scheme of intermittent treatment, such as giving doses of streptomycin every third day (Tucker, 1949), might be more effective, but the success of combined streptomycin and para-aminosalicylic acid therapy in reducing the incidence of streptomycin-resistant strains (Medical Research Council, 1949) makes it improbable that any scheme which employs streptomycin alone will now be tried. Our impression that some cases deteriorated during rest periods is an additional argument against the intermittent treatment. The clinical results in the trial, so far as one can generalize from such small numbers, suggest that a single injection of 1 g. of streptomycin a day is as effective as 0.25 g. six-hourly, and is preferred by the patient.

It will be recalled that we found some slight relation between, on the one hand, the time of resistance emergence and its degree, and, on the other, the condition of the patient before treatment and his response to streptomycin. It seems possible that such relation as has been observed is merely due to the temperature, radiographic appearance, and so on, being indirect reflections of the factors directly concerned. These factors might be such things as the size of the total population of tubercle bacilli in the lungs, the size of local concentrations of bacilli, the physical condition in the lung, or the patient's capacity to resist the disease.

The analysis of the results of routine sputum examination suggests that these may be of some use to the clinician in the management of the case, as the eight-weeks delay makes the routine streptomycin sensitivity tests of little day-to-day use. Quantitative studies have been made of the streptomycin sensitivity of the population of tubercle bacilli in the sputum of a number of our cases. These studies are being published elsewhere (Mitchison, 1950). Suffice it to say here that the results are in general accord with those obtained by routine methods.

## Summary

An attempt has been made to avoid or delay the emergence of streptomycin-resistant tubercle bacilli by schemes of intermittent dosage. Forty-five cases of acute progressive bilateral tuberculosis in young people were allotted at random to one of four dosage groups: (1) 0.5 g. of streptomycin six-hourly in alternate weeks; (2) 0.5 g. of streptomycin six-hourly in alternate months; (3) 0.25 g. of streptomycin six-hourly without intermission; and (4) 1 g. of streptomycin in a single daily dose without intermission. There was no evidence that any of the four dosage schemes delayed or avoided the emergence of streptomycin-resistant tubercle bacilli. Nor was there any

difference between the groups in the degree of streptomycin resistance shown by the bacilli.

It is concluded that 1 g. of streptomycin a day in a single injection, without intermission of treatment, is the most satisfactory way of giving the drug in pulmonary tuberculosis.

The relation of the emergence of streptomycin-resistant tubercle bacilli to the positivity of the sputum, and to various other factors, has been examined.

We are grateful to Dr. J. O. Irwin for assistance in the design of this trial; to Dr. L. G. Blair, who kindly made the radiographic assessments; and to the nursing staff of Brompton and Colindale Hospitals, who cheerfully undertook the added burden of work.

REFERENCES

Jensen, K. A. (1949). *Acta tuberc. scand.*, Suppl. 21, 42.
Medical Research Council (1948a). *British Medical Journal*, 2, 769.
—— (1948b). *Lancet*, 2, 862.
—— (1949). Ibid., 2, 1237.
Mitchison, D. A. (1949). Ibid., 2, 694.
—— (1950). *Thorax*. In press.
Pyle, M. M. (1947). *Proc. Mayo Clin.*, 22, 465.
Tucker, W. B. (1949). *Amer. Rev. Tuberc.*, 60, 715.

# BORNHOLM DISEASE

BY

J. H. S. HOPKINS, M.B., Ch.B.

Bornholm disease, "epidemic myalgia," or "epidemic pleurodynia," has been recognized as a commonly occurring disease in the Scandinavian countries for about the last twenty years. It probably occurs equally often in this country, but, apart from the pioneering work of Pickles (1933, 1939), has been curiously neglected, though at an earlier stage outbreaks of what was described as epidemic pleurisy were recorded as having attacked nurses and patients in two children's hospitals in London (Williamson, 1924; Lloyd, 1924). It is not included in the teaching of many hospital medical schools, and it figures briefly, if at all, in textbooks.

It is recognized when it occurs in epidemics, but the single sporadic case, and the first one or two in an epidemic, are usually not diagnosed. The milder cases are often referred to as fibrositis, strained muscle, indigestion, or pleurodynia; the severer ones as pleurisy, atypical pneumonia, coronary thrombosis, mesenteric adenitis, appendicitis, or poliomyelitis—according to the presenting symptoms and the predilection of the physician. The lack of familiarity with the disease is such that, as Hamburger and McNeil (1947) have suggested, it was still possible in 1944 for an epidemic to be reported as a "new syndrome."

Clinical descriptions of the disease show considerable variations between case and case, and also between epidemic and epidemic. If one sums up what is common to the various descriptions one gets the following picture. Bornholm disease is a benign illness occurring both in epidemics and sporadically. It is usually febrile, and is characterized by pain—usually of a muscular type (frequently described "as though a muscle were strained") and of very variable intensity—felt typically on deep respiration, coughing, laughing, or movement, somewhere around the thorax or abdomen. In children the pain is usually entirely abdominal. As a rule there is at least some abdominal tenderness, and this is particularly likely to be situated just below the costal margin and the xiphisternum. There are no true signs of affection of the viscera, though such may be simulated. A coarse pleural rub may occur. The disease shows extreme variability in severity and presentation, so that while a mild case may have only some malaise and pain on deep respiration, others may present with a crippling pain of sudden onset; there may be a high fever, and possibly abdominal rigidity; rapid grunting respirations are described; headache may be prominent, and vomiting at the onset sometimes occurs.

The cause is almost certainly a virus infection. Observations which suggest that Bornholm disease may be related to infection with the Coxsackie group of viruses are described in the communication by Findlay and Howard in this issue of the *Journal*.

The morbid anatomy has not been finally elucidated. It was thought originally by Sylvest (1932, 1934) to be an inflammatory condition of the muscular system. However, Locke and Farnsworth (1936) point out that "a very important quality of the pain is its direct relationship to sneezing, coughing, laughing, deep breathing, and especially exercise—that is, anything that causes movement of the diaphragm." They go on to point out that the areas in which the muscular pains are felt are those in which Capps (1932) has shown that pain is felt when referred from the diaphragm; and they suggest that the inflammation is at least primarily in the diaphragm. Further observation is required concerning whether only the diaphragm is attacked (the other muscles suffering from reflex irritation and spasm) or whether the other muscles themselves are involved in the inflammatory process.

Scadding (1946), on the other hand, on the basis of one in three of his cases having had a pleural rub, regarded the lesion as primarily a pleurisy, suggesting that possibly his cases were of a disease differing from but related to Bornholm disease; he named it "acute benign dry pleurisy," thus returning to the nomenclature of Williamson (1924) and Lloyd (1924). There does not seem sufficient justification for this in view of the fact that pleurisy is known to occur as a complication of Bornholm disease, and that Locke and Farnsworth found a pleural rub in one in seven of their cases. (It does seem that in certain epidemics a pleural rub occurs more often than in others.)

The common occurrence of tenderness just below the costal margin and xiphisternum (where the diaphragm is partly inserted into the aponeurosis of the abdominal muscles) and of pain in the shoulder-tip suggests that Locke and Farnsworth's view is probably correct, and that pleurisy, when it occurs, is a complication, due to extension of the inflammatory process to the adjacent pleura.

It should be noted that abdominal tenderness may occur in one of two distinct areas: (1) just below the costal margin, due to tenderness of the underlying diaphragmatic insertion; and (2) as referred pain, anywhere in the area supplied by the roots of D6–D12.

The epidemiology is somewhat similar to poliomyelitis, with maximum incidence in the late summer and autumn

## Illustrative Cases

The first seven cases described below occurred in one house consisting of two flats, every one of the occupants contracting the illness. They illustrate the diversity of presentation of illness, the children in general complaining of abdominal pain, the adults of pain on breathing. The dates of occurrence suggest an incubation period of not more than from four to eight days in these cases. Thus the first patient became ill on October 12, 1949, and the next two on October 16. Two further cases occurred on October 22, another on the 23rd, and the last on October 24. The interval between the first infection and the next two cases was therefore not more than four days. The next interval was six days. This is shorter than is usually reported.

*Case 1.*—M. H., who presumably introduced the infection, was a schoolboy, aged 8, who on October 12, 1949, said it hurt when he breathed. He was sent to school. Next day he had a temperature of 99.8° F. (37.7° C.); the pain was localized to the right abdomen and was still more painful on respiration. He did not appear ill. His appetite and bowel action were normal. There was tenderness in the right inguinal fossa, and the diagnosis was thought to be either retrocaecal appendicitis or mesenteric adenitis, the latter being more likely because of a palpable mesenteric gland. On the third day the abdominal symptoms had disappeared, but now he had headache, vomiting, and slight meningism. He then developed a mild lymphocytic meningitis, which subsided within a week, leaving no sequelae. (Lymphocytic meningitis has been described as an occasional complication of Bornholm disease. Lindberg, 1936; Gsell, 1949; Howard *et al.*, 1943).)

*Case 2.*—On October 16 B. H., aged 6, brother of M. H., felt unwell in the morning, was found to have a temperature of 100.6° F. (38.1° C.), and was put to bed. In the afternoon he began to complain of pain in the left upper quadrant of the abdomen, the pain being worse on breathing. Examination revealed nothing abnormal in the lungs. The abdomen generally was slightly tender and hyperaesthetic, especially in the left upper quadrant. The abdominal reflexes were diminished on the left. By the evening he was flushed and irritable, and looked toxic; the conjunctivae were congested. On the second day he woke up free from pain, much improved, and with a temperature of 99° F. (37.2° C.). There was nothing abnormal on examination. Next day he was apparently well, with a normal temperature. On the fourth and fifth days he had a symptomless temperature of 99° F., and on the sixth day was well.

*Case 3.*—On October 16, the same day as Case 2 became ill, N. S., aged 4, his playmate, woke up at 4 a.m. complaining of left upper abdominal pain. When I saw him later in the day the pain had gone and there was no abdominal tenderness, but his temperature was 101° F. (38.3° C.). As he was at that time convalescent from an attack of bronchitis and asthma, and as there were one or two rhonchi in his chest, I thought this was a recurrence of the bronchitis, and started him on a course of sulphamerazine. On the second day there was no cough, nor any symptoms or abnormal signs except a temperature of 99° F. (37.2° C.). Next day his temperature was normal, and the sulphamerazine was stopped. On the fourth day his temperature was 100° F. (37.8° C.), but he was still symptomless. On the next two days his temperature was 99°, and on the seventh day he was well.

*Case 4.*—On October 22 the father of M. H. and B. H. complained of vague aching subcostal pain, mainly on deep breathing and laughing; it was felt also in the left shoulder-tip. There was slight malaise and normal temperature. The only abnormal sign was tenderness in the epigastrium, mainly below the xiphisternum. Next day there was no pain, but his temperature was 99.2° F. (37.3° C.) in the evening. On the third day his temperature was normal, but he had slight malaise, which remained for a day or two.

*Case 5.*—On October 22 the mother of N. S. developed almost the same symptoms as those of Case 4—that is, a subcostal ache, felt also in the left shoulder-tip and aggravated by deep breathing. Her temperature was normal. There was tenderness in the epigastrium. Next day she had a symptomless temperature of 99° F. By the third day the original pain had disappeared, but there was an increase in malaise, with severe muscular pains across the back in the scapular regions, though no local tenderness could be elicited. The temperature was normal. During the following two days the back pains gradually became less, and on the sixth day she was well.

*Case 6.*—On October 23 the wife of Case 4 developed a very similar condition to her husband's, lasting for three days, and with a maximum temperature of 99.3° F. (37.35° C.).

*Case 7.*—On October 24 the husband of Case 5 developed the illness, the course resembling that of his wife—first with subcostal pain and tenderness on breathing, and on the second and third days with myalgic pains in the back. The maximum temperature was 99.4° F. (37.4° C.).

With Case 7 everybody in the two flats had had the illness. It was only half-way through the outbreak that I realized what the diagnosis was. On making inquiries at the school attended by M. H. I found that two boys were absent about the same time as he was—one with "atypical pneumonia," the other with "glandular fever." Through the kindness of their doctors I obtained the following histories.

*Case 8.*—On October 7 P. B., aged 9, developed a pyrexial illness with pain on breathing and upper abdominal tenderness. His father, who was a doctor, called in a consultant, who, on minimal signs (diminished breath sounds at one base), diagnosed atypical pneumonia. A radiograph was negative. Recovery occurred in a few days with sulphonamides and penicillin.

*Case 9.*—On October 17 C. R., aged 9, developed pain on breathing in the lower part of his chest, at first on the left and later on the right, with rapid respiration. His doctor "thought he had a pleural rub." A chest radiograph was negative. He later developed pain across the shoulders and eventually a generalized glandular enlargement, upon which a consultant was called in; he diagnosed glandular fever. A blood count on October 25 showed 9.5% monocytes, a Paul–Bunnell test being negative. The condition subsided in 14 days, the pyrexial condition lasting for about 10. It seems probable that this was a further case of Bornholm disease, complicated by lymph-node enlargement of uncertain aetiology.

## Subsequent Cases

Since the above cases, in one month I have come across the following cases in my practice.

*Case 10.*—A housewife from another part of London had awakened at 3 a.m. one day with "indigestion." The next morning she could hardly walk; she said it felt as though she had strained a muscle in her epigastrium, which was tender. On October 26, three days later, when I saw her, she felt pain "all over the back" on moving and breathing. Her temperature and pulse were normal, and there was no pleural rub. On the 27th she felt pain across the front of her chest, in her breasts, and across her back: "every breath hurt." There were still no abnormal physical signs. Next day she was well.

*Case 11.*—On October 27 a boy aged 10, in the same neighbourhood as the other cases, said that 36 hours previously he had begun to feel a pain, worse on breathing, along the right costal margin and in the R.I.F. He had felt ill at the onset, but had continued to attend school. When I saw him he had almost recovered and had no abnormal signs.

*Case 12.*—A barman, working in London, on November 14 complained of malaise, feverishness, headache, backache, and stiffness in his legs. He was seen on the 15th, when he had pain on both sides of his thorax, aggravated by deep breathing. His temperature was 98° F. (36.7° C.). There was no pleural rub; slight tenderness was present below both costal margins, and especially the xiphisternum. On the third day his temperature was normal and the pain less. He was well on the fifth day.

*Case 13.*—A boy aged 14 complained on November 25 of pain in his left lower thorax, worse on running and deep breathing. Next day the pain was worse, he felt ill, and was off his food. There was no change on the third day. When I first saw him, on November 28, the pain was less, his temperature was 96° F. (35.6° C.), and he had no pleural rub; there was vague tenderness about the eleventh rib posteriorly, and in the left hypochondrium. He was well on November 30.

## Previous Cases

Since becoming familiar with the syndrome I have looked back over the last two years, and, from memory and notes, now realize that I have seen, but missed, many cases of Bornholm disease. The following representative cases show the confusion that may occur if the disease is not kept in mind.

*Case 14.*—About two years ago I myself developed pain on respiration and movement somewhere in the mid-trunk, which I felt to be diaphragmatic, because it was clearly referred to the shoulder-tip. I felt ill, and thought it was pleurisy, probably tuberculous; I intended to see somebody about it, but in two days it was gone, and I had forgotten about it until the second attack.

*Case 15.*—In September, 1949, a girl of 5 was brought to see me, complaining of right-sided abdominal pain. The pain was worse on breathing; her temperature was 99.6° F. (37.55° C.), and there was an area of tenderness to the right of the umbilicus. I sent her into hospital for observation, and she was discharged a few days later, diagnosed by a process of exclusion, rather than by any positive evidence, as "? mesenteric adenitis."

*Case 16.*—In June, 1949, I was asked by another practitioner to see an adult whose history was that two days previously he had awakened with epigastric discomfort. He thought "he had strained a muscle." He later played nine holes of golf and then gave up because of the pain and retired to bed. The pain was worse on stooping, belching, and deep breathing. He had been pyrexial for two days when I saw him. His temperature was then 99° F. (37.2° C.). There were no abnormal physical signs in his chest, but there was a typical area of tenderness just below the xiphisternum. We sent him to hospital, where his case was diagnosed as "? strained muscle, ? upper respiratory infection," though there was no cough. However, a radiograph showed an area of decreased translucency at the right base consistent with either consolidation or collapse, and he was discharged three days later with a diagnosis of lobar pneumonia. A repeat radiograph a week or two later showed a clear lung field.

While Case 16 might, on the *x*-ray findings, be regarded as a virus pneumonia, the onset and symptoms are typical of Bornholm disease, as is also the epigastric tenderness: these, coupled with the absence of any cough, suggest that this was probably a case of Bornholm disease with lobar collapse (a complication which has been described).

*Case 17.*—In May, 1949, a man sent for me in the middle of the night, complaining of severe right-sided abdominal pain, worse on deep breathing and laughing, which had begun two days previously. I could detect nothing abnormal on examination, and endeavoured to reassure him. The pain persisted during the day, and I called in a consultant. The temperature was normal, there was no tenderness in the R.I.F., but it was thought he was slightly tender per rectum. He was sent to hospital as a possible case of acute appendicitis; laparotomy, however, revealed a normal appendix and no cause for his pain. He made an uneventful recovery.

*Case 18.*—In July, 1948, I saw a youth with pyrexia and pain and tenderness in his left loin and subcostal region. It was worse on respiration. There were no abnormal signs in his chest, and the urine was normal. One wondered at first whether it might be a case of perinephric abscess, but he was never seriously ill and made a quick recovery. He later saw a consultant, who on the history diagnosed pleurisy, and he was obliged to lead a restricted life for some months, on the basis of some *x*-ray changes in the lung fields.

*Case 19.*—In August, 1948, a man complained of severe pain in the lower chest. He said that every time he took a deep breath it tightened up round him like a belt. There were no abnormal signs in the chest. He was pyrexial for about a week, and was sent to hospital, whence he was discharged two weeks later with the bizarre diagnosis of "prolapse of a thoracic intervertebral disk."

## Comment

These cases are described to illustrate the extent of the variability of the disease. Mostly they are relatively mild cases, in contrast to the severer type of case usually described in the literature, where one meets with such phrases as "an anxious expression and stiff abdomen" (Ord, 1948) or "a violent pain arising suddenly in the lower thorax" (*Lancet*, 1946). The importance of the disease lies not so much in itself as in its potential mimicry, to those unfamiliar with it, of other severer illnesses. Case 17 was subjected to laparotomy, Case 18 to prolonged observation as a suspected case of tuberculosis, and Case 8 was subjected unnecessarily to sulphonamides and penicillin. Similar mistakes of diagnosis abound in the literature. The differential diagnosis is not so difficult as has been suggested. It is only necessary that the disease be borne in mind. Those cases which present with right-sided abdominal pain, and which are often confused with appendicitis, differ from it in that (1) they do not have the typical onset of appendicitis, and (2) patients are nearly always quite definite that the pain is worse on deep breathing, whereas in appendicitis this does not occur until the development of peritonitis. Similarly, in mesenteric adenitis the pain is not worse on breathing.

The diagnosis from pleurisy originating in the lung can be made on the more pronounced general myalgia and abdominal tenderness, and on the curious lack of association between the severity of the pain and the loudness of the pleural rub. Other cases with a muscular type of pain may suggest the pre-paralytic stage of poliomyelitis. In these it may be possible to form an opinion only from the typical distribution of the pain and the course of the illness.

The commonness or otherwise of the disease in this country is difficult to assess. Several epidemics have been described. The disease was comparatively unknown in Denmark until Sylvest began to publish his observations, as a result of which it became notifiable and was found to be occurring at the rate of several thousand cases a year. In view of the number of cases seen here in one practice in two years it seems not unlikely that there is a similar incidence in this country.


## Summary

Several cases of Bornholm disease are described. It is suggested that the disease occurs commonly in this country, but is often unrecognized.


## References


Capps, J. A. (1932). *An Experimental and Clinical Study of Pain in the Pleura, Pericardium, and Peritoneum.* New York.
Findlay, G. M., and Howard, E. M. (1950). *British Medical Journal*, **1**, 1233.
Gsell, O. (1949). *Schweiz. med. Wschr.*, **79**, 241.
Hamburger, H. J., and McNeil, C. (1947). *Lancet*, **2**, 784.
Howard, T., Weymuller, C. A., Edson, J., Ittner, E., Watson, J., and Cassidy, M. L. (1943). *J. Amer. med. Ass.*, **121**, 925.
Jamieson, W. M., and Prinsley, D. M. (1947). *British Medical Journal*, **2**, 47.
*Lancet* (1946). Annotation, **1**, 243.
Lindberg, G. (1936). *Acta paediat. Stockh.*, **19**, 1.
Lloyd, E. I. (1924). *Lancet*, **2**, 272.
Locke, E. A., and Farnsworth, D. L. (1936). *Trans. Ass. Amer. Phys.*, **51**, 399.
Ord, A. F. T. (1948). *British Medical Journal*, **2**, 916.
Pickles, W. N. (1933). Ibid., **2**, 817.
—— (1939). *Epidemiology in Country Practice*. Bristol.
Ronald, J. (1942). *J. R. nav. med. Serv.*, **28**, 144.
Scadding, J. G. (1946). *Lancet*, **1**, 763.
Sylvest, E. (1932). *Bull. Off. int. Hyg. Publ.*, **24**, 1431.
—— (1934). *Epidemic Myalgia*. London.
Williamson, B. (1924). *Lancet*, **2**, 64.


Under the 1950 Lord Memorial Essay Competition, founded in memory of the late Dr. J. R. Lord, the National Association for Mental Health offers certificated mental nurses a prize of £5 and a medal for the best essay on "What Satisfaction would Mental Nurses Gain from Exercising to the Full their Personal Talents and Professional Skills?" The closing date is August 31, and particulars may be obtained from the association at Maurice Craig House, 39, Queen Anne Street, London, W.1.

# COXSACKIE VIRUSES AND BORNHOLM DISEASE

BY

G. M. FINDLAY, C.B.E., Sc.D., M.D., F.R.C.P.

AND

ELSIE M. HOWARD

*Pharmacology Laboratories of the School of Pharmacy, Bloomsbury Square, London*

In the United States of America and in Canada viruses have been isolated which have been called Coxsackie viruses, from the village of Coxsackie in New York State, where the first known patients resided. The patients from whose stools, blood, or nasal washings the viruses have been obtained have been variously diagnosed as cases of non-paralytic poliomyelitis (Dalldorf and Sickles, 1948; Dalldorf *et al.*, 1949, Jaworski and West, 1949), "summer-grippe" (Melnick *et al.*, 1950), or epidemic myalgia (Curnen *et al.*, 1949). In Canada, Armstrong *et al.* (1950) have isolated the virus from the stools of three children from whom typical poliomyelitis virus was also recovered, from adults in contact with these children, and from a child suffering from a Guillain-Barré syndrome with an ascending Landry type of paralysis.

In some cases both a poliomyelitis and a Coxsackie virus have thus been isolated from the stools of the same patient. The Coxsackie viruses have been isolated not only from stools, blood, and throat swabs, but from sewage and flies.

There seem to be at least five strains of Coxsackie virus present in the United States of America (Howitt and Benefield, 1950): these viruses can be differentiated by a complement-fixation reaction as well as by the neutralizing effect of specific virucidal antibodies.

The Coxsackie viruses are transmissible only to suckling mice and hamsters, which develop paralysis after an incubation period which may be as short as 48 hours. The muscles of infected mice and hamsters exhibit a proliferation of the cells of the sarcolemma sheaths with loss of striation in the muscle fibres: all the voluntary muscles of the body, as well as the diaphragm, show similar changes.

In this country there have been available to us one of the strains isolated in Connecticut by Melnick *et al.* (1949), and three strains known as Dalldorf viruses 1, 2, and 3. We are indebted to Professor Sven Gard, of Stockholm, Dr. F. O. MacCallum, and Dr. J. A. Dudgeon for these viruses.

## A Laboratory Infection

During the course of investigations to determine whether there was evidence of interference between the Coxsackie viruses and mouse-adapted strains of poliomyelitis virus a laboratory infection occurred.

E. M. H. had been working with the Coxsackie virus for some three months. On January 3, 1950, towards the evening, she felt pain over the lower left ribs, particularly towards the back. This pain was worse on breathing and became more severe during the night. On the second day of illness the pain was very severe over the lower intercostal spaces on the left side. She found it difficult to breathe. There was no headache, but throughout the day the temperature varied between 99° and 100° F. (37.2° and 37.8° C.). At 2 p.m. it was 99.4° F. (37.4° C.), but at 6.30 p.m it had fallen to normal. During the third day the patient was afebrile and the severity of the muscular pain gradually decreased. On the fourth day there were no symptoms, but on the fifth day there was a slight but definite return of the muscular symptoms, without, however, a rise in temperature.

On the evening of the second day, when the patient had become afebrile, blood was removed and inoculated intraperitoneally into suckling mice. These mice remained in good health. A complement-fixation test on this serum for immunity to the Coxsackie virus was negative, but a further test on the fourth day after the onset of symptoms gave positive fixation with Coxsackie virus 2, the strain with which most work was being carried out.

A volunteer, whose serum on numerous occasions had given a negative complement-fixation for Coxsackie viruses, was then inoculated intranasally with 0.5 ml. of a 1 in 100 suspension of suckling mice in saline infected with Coxsackie virus 2 and filtered through a Seitz filtrate. This filtrate was active in suckling mice up to a dilution of $10^{-7}$.

No symptoms occurred till 46 hours after the intranasal instillation, when a sudden pain was felt in the intercostal spaces immediately below the point of the right scapula. The pain radiated round the intercostal space: it was more intense on taking a deep breath or laughing, and no position could be assumed in which the pain was completely alleviated. There was no nasal catarrh, and no headache or aching in the limbs apart from the intercostal pain. On the evening of the first day of illness, twelve hours after the onset of pain, the temperature was 99.2° F. (37.3° C.), but on the following morning, after a somewhat uncomfortable night, it was subnormal and the pain was easier. It continued for a further 48 hours and did not recur.

The complement-fixation reaction 24 hours after the onset of symptoms was still negative, but 72 hours after the onset complement-fixing antibodies were detectable in the serum: they have persisted for a period of nine weeks.

In connexion with these infections it is of some interest that two other possible infections have occurred in laboratories in this country to which the Coxsackie virus 2 has been supplied.

In a laboratory in the North of England infected material was handled by a pathologist on February 23 and 24, 1950. On February 28 he felt slightly cold, and severe pain developed round the lower part of the chest on the right side. There was also slight aching in the joints, but the chest pain was the main symptom; it was more severe on breathing or on any sudden movement. The temperature was 99° F. (37.2° C.). The symptoms continued unabated during the next 24 hours and the temperature rose to 104.6° F. (40.3° C.): this rise may have been due to the flaring up of a right maxillary antrum infection, from which the patient had suffered on previous occasions. The patient's blood culture was bacteriologically sterile and no malaria parasites were found in blood films. The symptoms gradually disappeared on March 2 and 3, the temperature being normal on the latter date. On the first day of illness the red cells were 5,500,000 per c.mm.; haemoglobin, 96%; leucocytes 16,100 per c.mm. (polymorphonuclear leucocytes 86%, small lymphocytes 9%, mononuclear cells 4%, eosinophils 1%).

The attack was diagnosed as most probably Bornholm disease, though at the time the patient was not aware of any possible association between Coxsackie virus and the symptoms of Bornholm disease. On the twenty-second day after the onset of symptoms the patient's serum when tested gave a positive complement-fixation reaction with Coxsackie virus 2.

In view of this finding it appeared to be of interest to examine the sera of workers in another laboratory in London where Coxsackie virus 2 had been handled. Of seven sera submitted to the complement-fixation test six were negative for both Coxsackie viruses 1 and 2, but one gave a positive reaction in a dilution of 1 in 20 with Coxsackie virus 2. The donor of the positive serum is unable to recall any illness during the past year which could account for his positive complement-fixation reaction. It is thus possible that he had suffered from a subclinical infection with Coxsackie virus 2, but whether this infection

was contracted during the course of laboratory investigations cannot now be ascertained.

### The Complement-fixation Reaction

Complement-fixation tests have been carried out in America by Casals *et al.* (1949) and Howitt and Benefield (1950). The following technique has been employed by us. The antigen is prepared from suckling mice paralysed by an intraperitoneal injection of Coxsackie virus. The skin, viscera, and brain are removed, the carcasses are ground up, and saline is added to form a 5% suspension. The suspension is spun at 3,000 r.p.m. for 30 minutes. Dilutions of the patient's serum in saline are first inactivated for 30 minutes at 56° C. and 0.25 ml. of each dilution is added to 0.25 ml. of antigen, together with 0.25 ml. of complement so diluted as to contain 2 minimum haemolytic doses per volume. The mixtures are shaken and left at 4° C. overnight for from 16 to 18 hours; 0.25 ml. of a haemolytic system containing 2.5% of washed sheep cells and 5 minimum haemolytic doses of amboceptor per volume is added to each tube. The tubes are shaken and placed in the water bath at 37° C. until the tubes containing normal control serum are completely haemolysed.

In carrying out tests antigen prepared from normal non-infected suckling mice is used as well as from the Coxsackie-infected mice. Known positive and known negative sera are always employed together with the sera to be tested. In order to eliminate any personal bias, sera from normal persons and from persons suspected of having had Coxsackie virus have been tested together, the particular sera from suspected infections being unknown to the person carrying out the tests.

In view of the similarity in symptoms between laboratory and experimental infections with Coxsackie virus 2 and those of Bornholm disease it appeared to be of interest to determine whether patients who had been involved in epidemics of Bornholm disease in this country had complement-fixing antibodies to the Coxsackie viruses.

Three small outbreaks of Bornholm disease are known to have occurred in the late autumn of 1949 in (1) Wensleydale, Yorkshire; (2) Richmond and Barnes, Surrey (Hopkins, 1950); and (3) Paddington, London, W.C.1 (Sylvester, 1950, unpublished observations). The results of tests on 18 patients involved in these three outbreaks are shown in

TABLE I.—*Complement Fixation by Coxsackie Virus 2 of Sera From Patients with a History of Epidemic Bornholm Disease*

| Epidemic | Patient | Complement Fixation | | |
|---|---|---|---|---|
| | | Coxsackie 2 Antigen | Coxsackie 1 Antigen | Normal Mouse Antigen |
| Wensleydale .. .. (Sept., 1949) | O.M. | 1 in 5 | 0 | 0 |
| | S.M. | 1 in 10 | 0 | 0 |
| | W.M. | 1 in 20 | 0 | 0 |
| Barnes and Richmond (Sept.-Oct., 1949) | J.H.S.H. | 1 in 80 | 0 | 0 |
| | M.H. | 1 in 40 | 0 | 0 |
| | A.H. | 1 in 40 | 0 | 0 |
| | A.B. | 1 in 5 | 0 | 0 |
| | J.I. | 1 in 5 | 0 | 0 |
| | O.N. | 1 in 10 | 0 | 0 |
| | D.W. | 1 in 5 | 0 | 0 |
| | M.W. | 1 in 5 | 0 | 0 |
| | M.S. | 1 in 5 | 0 | 0 |
| Paddington, London.. (Sept.-Oct., 1949) | G. | 1 in 20 | 0 | 0 |
| | S. | 1 in 20 | 0 | 0 |
| | H. | 1 in 20 | 0 | 0 |
| | W. | 1 in 20 | 0 | 0 |
| | K. | 1 in 5 | 0 | 0 |
| | B. | 1 in 5 | 0 | 0 |
| | H. | 1 in 20 | 0 | 0 |
| Aden, 1946 .. .. | D.M.P. | 1 in 20 | 0 | 0 |

Table I. It will be seen that all the sera gave positive results in dilutions of 1 in 5 to 1 in 80, the sera having been examined two to six months after the actual attack. One of the sera, that of M.H., was from a boy whose case is described by Dr. J. H. S. Hopkins in this issue of the *Journal*; he had had meningitic symptoms, which might well have been mistaken for non-paralytic poliomyelitis. D.M.P. was involved in an outbreak in Aden in 1946 (Jamieson and Prinsley, 1947).

In Table II are shown the results of testing sera from persons who had given a history of acute pain in the lower thoracic region resembling that encountered in Bornholm

TABLE II.—*Complement Fixation by Coxsackie Virus 2 of Sera From Patients Not Associated with any Epidemic of Bornholm Disease But Having a Suggestive History*

| Patient | Date of Illness | Location | Complement Fixation | | |
|---|---|---|---|---|---|
| | | | Coxsackie 2 Antigen | Coxsackie 1 Antigen | Normal Mouse Antigen |
| Mrs. J. | March, 1950 | Barnes | 1 in 5 | 0 | 0 |
| E. | June, 1949 | ,, | 1 in 10 | 0 | 0 |
| J. | Aug., 1949 | ,, | 1 in 5 | 0 | 0 |
| T.H.D. | Feb., 1949 | Liverpool | 1 in 10 | 0 | 0 |
| D. | Dec., 1949 | ,, | 1 in 20 | 0 | 0 |
| B. | Sept., 1949 | Cumberland | 1 in 20 | 0 | 0 |
| D. | ,, | ,, | 1 in 20 | 0 | 0 |
| H. | ,, | ,, | 1 in 10 | 0 | 0 |
| B. | Feb., 1950 | Manchester | 1 in 10 | 0 | 0 |
| F. | March, 1950 | ,, | 1 in 10 | 0 | 0 |
| M.F. | Dec., 1942 | Hertfordshire | 0 | 0 | 0 |
| N.Y. | March, 1950 | Northants | 1 in 20 | 0 | 0 |
| J.Y. | ,, | ,, | 1 in 20 | 0 | 0 |
| E.Y. | No illness | ,, | 0 | 0 | 0 |
| D.Y. | ,, ,, | ,, | 1 in 10 | 0 | 0 |
| J.Y. | ,, ,, | ,, | 1 in 10 | 0 | 0 |

disease: all were positive against Coxsackie virus 2 except one whose attack had occurred eight years previously. Mrs. J.'s first serum was obtained on the fourth day of illness, when complement fixation was positive in a dilution of 1 in 5: a second specimen, obtained on the 15th day of illness, showed positive complement fixation in a dilution of 1 in 10 and a specimen six weeks later 1 in 20. The early occurrence of complement fixation in an apparently sporadic case of Bornholm disease is of interest, since Howitt and Benefield (1950) have noted the presence of complement-fixing antibodies to Coxsackie viruses two, four, four, and five days after the onset of illness, and in an experimental infection in this country complement fixation became positive on the third day after the onset of symptoms. N.Y. and J.Y., two brothers aged 5 and 7, were diagnosed as cases of non-paralytic poliomyelitis, or possibly influenza, but showed no evidence of a rise in titre for influenza viruses. N.Y. had a temperature of 103° F. (39.4° C.) with vomiting and twitching of the facial muscles: J.Y. had a temperature of 99° F. (37.2° C.), with pain in the right hip and twitching of the facial muscles. The sera of the father, mother, and grandfather were negative, but the sera of two other brothers, aged 6 and 13 years, who occupied the same bed as N.Y., were positive although they had had no illness. Cases of true paralytic paralysis had occurred in the same town previously. D.M.P., who had suffered from symptoms suggestive of epidemic myalgia in 1946 when in Aden, was also positive. The complement-fixation reaction given by the serum of T.H.D. is of some interest, since his attack of intercostal pain on the left side was diagnosed and treated as being due to coronary thrombosis.

In addition to the sera reported in Tables I and II six sera from patients diagnosed as suffering from non-paralytic poliomyelitis or lymphocytic meningitis have been examined with negative results; similar negative results have been obtained with the sera of 26 healthy persons giving no history of symptoms suggesting Bornholm disease.

The specificity of the complement-fixation test for Coxsackie viruses has been further examined by testing sera

known to contain antibodies against influenza A and B viruses, or from persons immune to mouse-adapted poliomyelitis viruses, Lansing and M.E.F. 1 strains; Columbia SK virus; meningo-encephalomyelitis; yellow fever; Rift Valley fever; mumps; infective hepatitis; and herpes simplex. Boiling the antigen for five minutes destroys all complement fixation, but heating the antigen for one hour at 56° C. leaves some complement-fixing activity. The filtrate, after passing a suspension of the virus through a gradocol membrane of 31 $\mu\mu$ bore size which retains the virus, still has some complement-fixing action. It thus seems probable that the complement-fixation reaction depends on a soluble-specific substance and not on the virus itself.

Although adult mice do not develop any symptoms suggestive of infection, it has been found that the muscles of adult mice inoculated intraperitoneally three days previously contain sufficient antigen to allow of their being used in the complement-fixation test: on inoculation of a suspension of this adult muscle into suckling mice no infection occurred.

In a small number of cases virus-neutralization tests have been carried out in suckling mice with sera from known Coxsackie virus 2 infections and from cases clinically diagnosed as Bornholm disease: the results parallel those of the complement-fixation test.

Haemagglutination tests using Group O human red cells and the red cells of chickens, pigeons, mice, rats, guinea-pigs, hamsters, and frogs have all been negative. This is in conformity with the negative results obtained by Casals *et al.* (1949).

## Discussion

These investigations show that symptoms of myalgia resembling those seen in Bornholm disease (also known as epidemic myalgia, epidemic myositis, epidemic pleurodynia, epidemic pleurisy) occurred in laboratory personnel during investigations with Coxsackie virus 2 and are followed in a few days by the appearance of positive complement-fixing antibodies in the blood.

Coxsackie virus 2 can infect when instilled intranasally, the incubation period being 46 hours: the symptoms resemble those of epidemic myalgia. Here again complement-fixing antibodies and virus-neutralizing antibodies appeared in the serum three days after the onset of symptoms.

Sera from patients involved in three outbreaks diagnosed as Bornholm disease in Barnes and Richmond, Surrey, in West London, and in Yorkshire all fix complement with Coxsackie virus 2 and neutralize this virus, whereas they show no reactions with Coxsackie virus 1 or 3 or with normal mouse antigen. Complement-fixing antigen was present in the serum of a sporadic case of epidemic myalgia as early as the fourth day of infection.

One patient with symptoms of abdominal pain and lymphocytic meningitis has shown complement-fixing antibodies with Coxsackie virus 2. Other patients not associated with an epidemic of Bornholm disease have shown complement-fixing antibodies after a history of sudden myalgia in the chest. These patients have been variously diagnosed as sporadic cases of Bornholm disease, coronary thrombosis, non-paralytic poliomyelitis, and intercostal neuralgia, and have been scattered throughout England from Cumberland to Surrey. The sera of two brothers who had had no illness gave a positive complement fixation: they had occupied the same bed as their brother, who was positive and had been thought to have non-paralytic poliomyelitis.

The activity of the Coxsackie virus antigen is destroyed by boiling for five minutes; it is reduced by heating at 56° C. for one hour, but is not entirely destroyed. So far as complement fixation goes, Coxsackie 2 and the Melnick strain examined by us appear to be closely related. It is not improbable that strains of Coxsackie virus 2 are present in this country, and their presence in cases of non-paralytic poliomyelitis requires further study. The occurrence of meningitic symptoms in epidemics of Bornholm disease has been not infrequently reported (McConnell, 1945; Gsell, 1949).

While this communication was in the press a virus closely resembling Coxsackie virus 2 was isolated from the blood, stools, and nasal washings of a patient who had developed typical symptoms of Bornholm disease 52 hours previously: complement-fixing antibodies for Coxsackie virus 2 were present in his blood at this period. In addition complement-fixing antibodies against Coxsackie virus 1 have been found in the blood of adults recovered from Bornholm disease in Hertfordshire, and in the blood of an adult resident in Versailles, France: two children from Northamptonshire, diagnosed as possibly non-paralytic poliomyelitis, have also fixed complement with Coxsackie virus 1 but not Coxsackie virus 2.

## Conclusions

Coxsackie virus 2 can infect the adult intranasally, producing symptoms resembling those of Bornholm disease.

Coxsackie virus 2 has been isolated from the nasal washings and blood of an adult with Bornholm disease.

Complement-fixing antibodies and virus-neutralizing antibodies develop within three days of the onset of symptoms after experimental infection.

Patients from epidemics of Bornholm disease in England and Aden show complement-fixing and virus-neutralizing antibodies against Coxsackie viruses 1 or 2 but not against Coxsackie virus 3. Such antibodies are present by the third day of infection and may show an increase in titre.

Some cases of Bornholm disease with lymphocytic meningitis have complement-fixing antibodies against Coxsackie virus 2.

Sporadic cases with pain in the chest, with various diagnoses including non-paralytic poliomyelitis and coronary thrombosis, have antibodies against Coxsackie viruses 1 or 2.

The evidence suggests that Coxsackie viruses 1 and 2 are widely distributed in Great Britain and that some epidemics of Bornholm disease in this country are associated with infection by Coxsackie virus 1 or 2 or very closely allied viruses.

Our thanks are due to all those who have supplied sera, more especially Dr. W. N. Pickles, Dr. J. H. S. Hopkins, Dr. D. Sylvester, Dr. F. Himmelweit, Dr. C. H. Andrewes, Dr. Chu, Dr. F. S. Panton, Dr. Rhodes Allison, Dr. H. J. Voss, Dr. F. Bentham, Dr. G. Dick, and Professor B. G. Maegraith.

The work was carried out in the laboratories of Professor G. A. H. Buttle, to whom we wish to express our gratitude. One of us (G. M. F.) is in receipt of an expenses grant from the Medical Research Council.

### References

Armstrong, N. P., Wilson, F. H., McLean, W. J., Silverthorne, N., Clark, E. M., Rhodes, A. J., Knowles, D. S., Ritchie, R. C., and Donohue, W. L. (1950). *Canad. J. publ. Hlth*, **41**, 51.

Casals, J., Olitsky, P. K., and Murphy, L. C. (1949). *Proc. Soc. exp. Biol., N.Y.*, **72**, 636.

Curnen, E. C., Shaw, E. W., and Melnick, J. L. (1949). *J. Amer. med. Ass.*, **141**, 894.

Dalldorf, G., and Sickles, G. M. (1948). *Science*, **108**, 61.

—— —— Plager, H., and Gifford, R. (1949). *J. exp. Med.*, **89**, 567.

Gsell, O. (1949). *Schweiz. med. Wschr.*, **79**, 241.

Hopkins, J. H. S. (1950). *British Medical Journal*, **1**, 1230.
Howitt, B. F., and Benefield, U. R. (1950). *Proc. Soc. exp. Biol., N.Y.*, **73**, 90.
Jamieson, W. M., and Prinsley, D. M. (1947). *British Medical Journal* **2**, 47.
Jaworski, A. A., and West, E. J. (1949). *J. Amer. med. Ass.*, **141**, 902.
McConnell, J. (1945). *Amer. J. med. Sci.*, **209**, 41.
Melnick, J. L., Ledinko, N., Kaplan, A. S., and Kraft, L. M. (1950). *J. exp. Med.*, **91**, 185.
—— Shaw, E. W., and Curnen, E. C. (1949). *Proc. Soc. exp. Biol., N.Y.*, **71**, 344.

# ABACTERIAL FORM OF ENDOCARDITIS WITH NECROSIS OF THE EARS

BY

**KEITH BALL, M.D., M.R.C.P.**

*Senior Registrar, Central Middlesex Hospital*

The case here reported, in which symmetrical necrosis affected the ears of a patient with the clinical features of subacute bacterial endocarditis, will be found of interest. Repeatedly negative blood cultures, failure to respond to penicillin, myocardial infarction, and death in uraemia were other unusual features.

## Case Report

A labourer aged 30 was admitted to hospital on February 27, 1947. He had had rheumatic fever at the age of 6 and schizophrenia at 25. In August, 1946, he had been admitted to St. Mary Abbots Hospital complaining of headaches, rigors, and pain and bleeding of both pinnae. He had an irregular fever and showed signs of mitral stenosis and aortic incompetence. Seven blood cultures were sterile. The haemoglobin was 83%; white blood cells varied from 5,000 to 8,000 per c.mm. (neutrophils 31–60%, lymphocytes 29–40%, monocytes 5–27%). The urine contained red blood cells and occasional hyaline and granular casts. He was treated with penicillin, 80,000 units three-hourly for seven weeks—a total of 31,000,000 units. Some lowering of the temperature occurred, but there was little improvement in the general condition, and he discharged himself from hospital on October 30, 1946.

On admission to the Central Middlesex Hospital he complained of malaise, anorexia, and rigors. Ten days previously he had developed a sudden pain in his left arm which spread to the left of the sternum and lasted two days.

Examination revealed clubbing of nails, healthy teeth, a small haemorrhage in the right fundus, and regular pulse. Blood pressure 150/60. The heart was not enlarged. There were signs of mitral stenosis and aortic incompetence. The liver and spleen were enlarged to three fingerbreadths below the costal margin, and the spleen was tender. On the left pinna a tender blue area with incipient necrosis was present.

*Investigations.*—Eight blood cultures taken between February 28 and April 3 were sterile. Aerobic and anaerobic cultures were maintained for 14 and in some cases 21 days. The urine contained albumin and many red blood cells. Blood urea rose from 66 to 274 mg. per 100 ml. Plasma proteins: albumin 3 g., globulin and fibrinogen 4.5 g. per 100 ml. Takata–Ara, + + +. Thymol turbidity test, 15 units. Serum colloidal gold reaction, + + + + +. Haemoglobin fell from 56% to 40%, and the white blood cells varied from 5,000 to 16,000 per c.mm. The sedimentation rate (Westergren) rose from 98 to 124 mm. per hour. The Wassermann reaction was negative. The urea clearance was 12% of normal. Serial electrocardiograms showed the characteristic appearances of a recent anterior cardiac infarction (Fig. 1). Biopsy from the left pinna on March 27 showed many greatly dilated capillaries, some of which contained small projections of endothelium-covered fibrinoid material. Full pathological details have been published by Pagel (1949).

A diagnosis of subacute infective endocarditis was made. The cardiac infarction was considered embolic in origin. The patient had an irregular fever up to 101° F. (38.3° C.) for the first six weeks. After the eight sterile blood cultures penicillin was started, 200,000 units being given every three hours for six weeks—a total of 70,400,000 units. Although his temperature became lower his general condition deteriorated. On April 13 he awoke with pain in the right pinna, which was found to be reddened and swollen, with mottled blue areas, and a few days later necrosis appeared. Meanwhile separation of the necrotic portion of the left pinna occurred (Fig. 2). He died in uraemia on June 10, 1947.

*Post-mortem Examination.*—The chief abnormal findings were as follows. *Heart*:—Weight, 460 g. (normal 300 g.). The aortic valve was bicuspid and showed a number of yellowish-red vegetations up to 0.5 cm. long, the largest of which lay close to the orifice of the left coronary artery. There was marked narrowing of the anterior descending branch of the left coronary artery 3 cm. from its origin. A healed infarct was present at the apex of the left ventricle. *Kidneys*:—right, 230 g.; left, 240 g. (normal 125–170 g.); flea-bitten appearance; scar of old infarct on left. *Liver*:—1,930 g. (normal 1,400–1,600 g.); well-marked nutmeg appearance. *Spleen*:—450 g. (normal 150–200 g.). *Brain*:—recent infarct in right parietal cortex and small cyst in right occipital lobe.

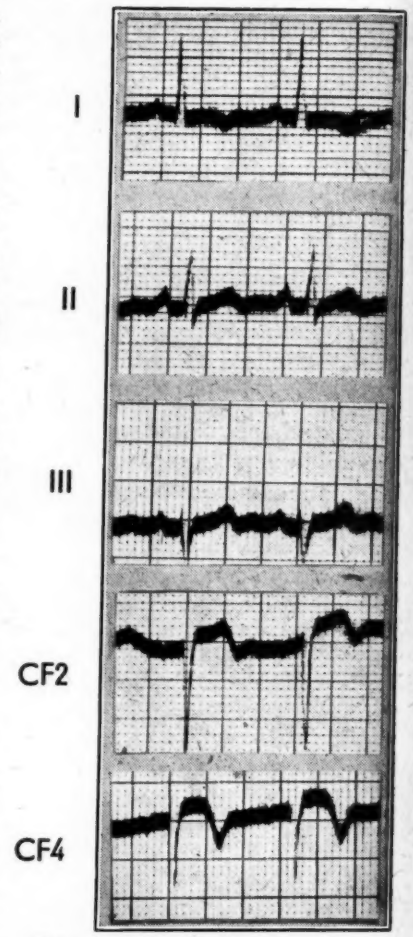



FIG. 1.—Electrocardiogram taken on March 4, 1947, showing changes of recent anterior cardiac infarction.

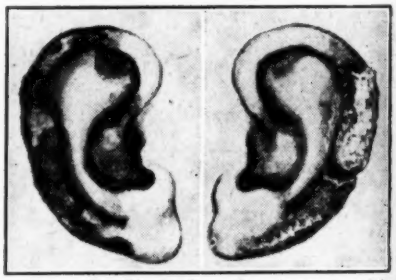


FIG. 2.—Necrosis of pinnae, with impending separation of the left pinna, April 28, 1947.

*Histology.—Aortic valve*:—Extensive red and white thrombotic vegetations. No bacteria seen in Gram preparation. *Myocardium*:—Fresh changes consisting of small focal areas of interstitial infiltration with polymorphs and mononuclear cells, presumably embolic in origin. Old changes presumed to be rheumatic, consisting of scars and small areas of perivascular fibrosis and calcification surrounded by a few multinucleated giant cells and lymphocytes. *Kidney*:—Most of the glomeruli showed patchy and chronic changes. Many of the tufts were partially replaced by connective tissue. Proliferative and endothelial changes were slight, and no crescents were seen. Interstitial fibrosis and patchy tubular atrophy were present. It

appeared to be a chronic process in which parts of the glomerular tufts had previously been the site of multiple embolic foci but had become fibrosed. Conclusion: chronic embolic nephritis.

## Discussion

The most striking feature of this case of endocarditis was the necrosis which affected the helix of each ear. Tender blue swellings first appeared, necrosis slowly developed, and separation of the dead tissue occurred later. The left ear, which had been affected on his first visit to hospital, appeared normal on his second visit, but later relapsed. This slowly developing and remitting process, which affected each ear in turn, was most unlike an embolic process, and the non-embolic nature of the condition was favoured by the histological appearances, which are discussed in detail by Pagel (1949). No similar cases of "acronecrosis" in subacute bacterial endocarditis have been found in the literature.

Cardiac infarction is a rare occurrence in this condition. Hamman (1941), reviewing 40 recorded cases of coronary embolism, found that bacterial endocarditis was the source of the embolism in 19 out of 38 cases in which the aetiology was stated. In most of the cases the diagnosis was only made at necropsy following sudden death. In the present case the characteristic electrocardiographic changes confirmed the diagnosis three months before death.

There were several other atypical features. (1) Progressive renal failure with death in uraemia is rare in subacute bacterial endocarditis. Fishburg (1939) states that the course of the disease is hardly ever modified by multiple glomerular embolization. Although glomerular nephritis may occur and cause uraemia, there was no histological evidence of this in the present case. The picture was one of chronic embolic nephritis. (2) The repeatedly sterile blood cultures. Seven were taken before his first course of penicillin and a further eight before the second course, but all fifteen were sterile. Although the inability to grow an organism cannot exclude bacterial endocarditis, it is unusual to get fifteen sterile cultures at a time when fever and haematuria indicate definite activity of the disease. Moreover, no organisms could be found in the vegetations at necropsy. (3) The signs of liver damage as shown by the liver function tests. (4) The failure to respond to penicillin. Although the temperature became lower, no clinical improvement occurred. Since the patient was given 1,600,000 units daily for six weeks and renal failure was present, a high blood level of the drug was probably reached.

Several authors have described a form of endocarditis in which persistently negative blood cultures occur although the clinical features resemble the bacterial form. Baehr (1931) found that 57 out of 161 cases of subacute bacterial endocarditis followed to necropsy were free from bacteria. Blood cultures were sterile and the vegetations contained no bacteria. Several Spanish authors have recently described a number of cases of "abacterial endocarditis" (de Bes *et al.*, 1946; Jimenez Diaz, 1946). They believe that bacterial and abacterial endocarditis are separate entities. Bacterial endocarditis is characterized by persistently positive blood cultures, a short clinical course without remissions, and a rapid response to penicillin. In abacterial endocarditis, on the other hand, the blood cultures are persistently negative, the course is more prolonged, with remissions, and there is a complete failure to respond to penicillin. Other features of this type are a raised plasma globulin, positive empirical liver-function tests, a higher sedimentation rate than is usually found in the bacterial form, and a greater enlargement of the liver and spleen. A renal course with albuminuria, haematuria, urinary casts, and renal failure may occur, and the outcome is always fatal. Of 67 cases described by Landazuri and his colleagues (1946), 25 were abacterial and the remainder bacterial. Camelin *et al.* (1947) and Donzelot *et al.* (1947) have described similar cases from France. Such a high percentage of cases with negative blood cultures contrasts with the experience of Bramwell (1948), who recovered an organism in 50 out of 52 cases.

In bacterial endocarditis the various pathological changes are attributed to bacterial emboli arising from the heart valves, but in abacterial cases such an explanation is clearly not possible. It has been suggested that a heightened immunity of the host accounts for the absence of bacteriaemia, and possibly for the visceral lesions as well. A retention of the bacteria in the tissues has also been put forward as an explanation. Whatever the real cause of this variety, it is important that it should be recognized, as there seems to be no doubt that it is a true clinical entity.

## Summary

A case of the abacterial form of endocarditis is described in which the following features occurred: symmetrical necrosis of the ears, cardiac infarction, liver damage, failure to respond to penicillin, and death in uraemia as a result of chronic "embolic" nephritis.

A review of the literature suggests that the abacterial form of endocarditis is a clinical entity.

I am grateful to Dr. Walter Pagel for the histological reports, to Mr. J. M. Milloy, medical superintendent of St. Mary Abbots Hospital, for lending me clinical records, and to Miss J. Dewe for the illustration.

### References

Baehr, G. (1931). *Trans. Ass. Amer. Phys.*, **46**, 87.
Bramwell, C. (1948). *Lancet*, **2**, 481.
Camelin, A., Garnung, H., Vigneau, and Forestier (1947). *Pr. méd.*, **55**, 870.
de Bes, L. T., Riera, J. G., and Tena, A. F. (1946). *Rev. clin. esp.*, **22**, 6.
Donzelot, E., Kaufmann, H., and Escalle, J. E. (1947). *La Maladie d'Osler*. L'Expansion Scientifique Française, Paris.
Fishburg, A. M. (1939). *Hypertension and Nephritis*, 4th ed., p. 551. Lea and Febiger, Philadelphia.
Hamman, L. (1941). *Amer. Heart J.*, **21**, 401.
Jimenez Diaz, C. (1946). *Rev. clin. esp.*, **22**, 493.
Landazuri, E. O. de, Iglesias, A. M., and Carro, J. P. (1946). Ibid., **22**, 396.
Pagel, W. (1949). *Amer. J. med. Sci.*, **218**, 425.

---

The American Society for the Prevention of Blindness has announced the results of a study of eye accidents in the schools in Louisville, Kentucky. The society estimates that American children suffer yearly 66,000 eye injuries, of which 750 are so serious that the patient loses the sight of an eye. Among Louisville children, an average of 117 eye accidents occurred annually. Boys suffered 75% of the injuries, though the number of boys and girls were approximately equal, and most of the accidents occurred in sports and play. To cut down the high accident rate among children four recommendations are made: (1) Prohibition of fireworks and weapons for children; these include air-rifles, bows and arrows, and sling shots. (2) Better supervision of play, to lessen the chances of children improvising unsafe games and using dangerous makeshift playthings. (3) Education of the children on hazards to the eye. (4) Incentives to make children more safety conscious, such as poster and essay contests and clubs. The main immediate causes of eye injuries, according to the report, are blows; accidental injuries with sharp objects such as pointed sticks, pens, and pencils; falls; foreign bodies; and fireworks. Air-guns and such toys accounted for 17% of the serious cases, and the society considers there is no longer an excuse for permitting children to play with them.

# DIPHTHERIA IN SOUTH PERSIA

BY

R. HODGSON, F.I.M.L.T.

AND

I. S. STEWART, M.B., Ch.B.

*Pathologist, Anglo-Iranian Oil Company Hospital, Abadan*

As we have been unable to trace any significant reference to diphtheria in Persia we give an account of the 48 cases which we encountered from January 1, 1948, to September 30, 1949, on Abadan Island, South Persia.

The island lies in the Shatt-el-Arab estuary, at the head of the Persian Gulf, is 25 miles long, and is 6 miles wide at its broadest point. The rivers Karun and Bahmanshir separate it from the mainland. Apart from a marginal belt of date palms it is a flat desert, nowhere more than 10 ft. (3 metres) above the level of the river. From May to the end of September it is extremely hot, with a maximum shade temperature ranging from 100° F. (37.8° C.) to a peak of 120° F. (48.9° C.) in June. The summer humidity is rarely above 30% before August, when the south wind from the Gulf raises it to 50%. The winter is cool, with occasional torrential rain-storms, providing the annual rainfall of 15–20 in. (38–51 cm.). The minimum night temperatures in winter fall to 33° F. (0.55° C.), but the summer nights have a minimum of around 93° F. (33.9° C.).

The population is about 200,000, and consists mainly of non-immunized Persians. The foreign elements fall into three groups: the British staff of the oil company and their families, numbering about 5,000; the Indians and Pakistanis, about 1,500; and a continually changing shipping population of about 1,000. At least 120,000 of the Persian population are either employed by the oil company or are members of the families of employees, the company assuming responsibility for their medical care. Cases of infectious disease arising among the remainder are received at the Company Isolation Hospital. It is therefore reasonable to assume that most of the cases of diphtheria are seen and treated. Mild cases of course may, as elsewhere, pass unnoticed.

Four or five ships enter and leave the port daily, coming from all parts of the globe, so that in theory infection may be introduced from any country. The travels of members of the staff on leave offer further possibilities. With its numerous outside contacts, therefore, it is probably not a suitable area on which to assess the incidence of the disease in South Persia as a whole, the inland areas being less open to the introduction of new strains.

The company's laboratory at Masjid-i-Suleiman, 130 miles inland, is the only other major source of information available to us. The records of the two laboratories (Table I) suggest that the disease was a rarity before 1948, but shortage of staff, both laboratory and medical, and restricted equipment probably give a false impression of the war years.

TABLE I.—*New Cases Reported After Isolation of C. Diphtheriae*

| | At Abadan | At Masjid-i-Suleiman |
|---|---|---|
| 1941 .. .. .. .. | 1 | 2 |
| 1942 .. .. .. .. | 2 | 4 |
| 1943 .. .. .. .. | 3 | 3 |
| 1944 .. .. .. .. | 0 | 0 |
| 1945 .. .. .. .. | 3 | 0 |
| 1946 .. .. .. .. | 0 | 3 |
| 1947 .. .. .. .. | 2 | 0 |
| 1948 .. .. .. .. | 24 | 3 |
| 1949 (9 months) .. .. | 17 | 4 |

The cases at Masjid-i-Suleiman are not referred to below, and are not included in the total of 48".

## Bacteriology

Before 1948 the diagnosis was made on films from an 18-hour culture on Löffler's inspissated serum, using Neisser's stain. The isolation of pure cultures was in consequence difficult, but several of the strains obtained proved virulent. In 1948 the following routine procedure was adopted.

The swab is inoculated on Neill's tellurite agar and on unheated rabbit-blood agar. A film is then made and Gram-stained, Vincent's organisms and *Oidium* being reported if present, but no opinion being given on the presence or absence of *Corynebacterium diphtheriae*. The two plates are examined after 18 hours' incubation, haemolytic streptococci being confirmed by stained films and a "rake through" film being stained by methylene blue to exclude *C. diphtheriae*. The blood plate is discarded, and the tellurite is examined again at 36 hours.

Colonies appearing to be *C. diphtheriae* on tellurite and showing bacillary forms with multiple bars in a methylene-blue film are reported immediately as "positive." Coccal forms giving colonies resembling mitis diphtheria have often been encountered. Subcultures from tellurite to heated blood agar and from that to Hiss's serum-water sugars and Hartley's broth have been made in all cases. Finally, an 18-hour culture on Löffler's serum is suspended in 2 ml. of distilled water and inoculated into the axilla of a guinea-pig weighing less than 250 g. Death of the animal in two days or less, with characteristic post-mortem change, has been accepted as evidence of virulence. When the animals are alive and well at the fifth day the strains have been reported as avirulent. Control guinea-pigs, immunized with antitoxin immediately before inoculation with living cultures, have not been used. The rapid death of the animals, with the post-mortem changes seen in guinea-pig diphtheria—namely, gelatinous exudate at the site of inoculation and in the pleural cavities, with haemorrhagic change in the suprarenals—does not seem to leave any doubt regarding the virulence of the organism.

## Types Encountered

The gravis type has been reported twice. Each strain gave a large "daisy-head" grey colony on tellurite, a "ground-glass" growth on heated blood agar, with characteristic morphology in a stained film, fermented glucose, and starch, but not saccharose, and was virulent for the guinea-pig. Growth in broth gave a deposit with clearing of the medium but no pellicle formation.

The mitis type has been reported 39 times. The colonies were from 1.5 to 3 mm. in diameter, smooth, shining, with a central papilla and an uninterrupted margin. Stained films gave a characteristic morphology. Glucose was fermented, but not starch or saccharose. All but two strains were "virulent" for the guinea-pig. One of these was isolated from the throat of a fatal case and the other from a symptomless individual in a household where a proved case had occurred. In only four cases has growth in broth given a uniform turbidity. The rest showed a granular appearance combined with turbidity and a certain amount of deposit. Growth on heated blood agar gave a "ground-glass" appearance, and in no case was any green formation noted about the colonies. Five strains were cultured on the special chocolate agar recommended by Gordon and Higginbottom (1942), but none of them showed any green formation in the medium.

The intermedius type has not been encountered.

*Haemolysis.*—In all cases in which haemolytic colonies have been observed at 18 hours on the unheated rabbit-blood agar, films have shown the colonies to be a streptococcus. Five mitis strains, tested by the method of Hammerschmidt, quoted by Anderson *et al.* (1931), showed haemolysis. To 1 ml. of a 48-hour culture in broth was added 1 ml. of 1% washed human red blood cells; this was then incubated two hours, placed overnight in the cold, and then read.

## Clinical Features

In Table II the bacteriological "positives" and also seven cases with convincing clinical evidence of the disease are shown. Further reference to the latter group will be made.

TABLE II

| | Recovered | Died | Fate Unknown | Total |
|---|---|---|---|---|
| Clinical diphtheria: positive swab | 20 | 7 | — | 27 |
| Symptoms slight: positive swab. Presumed carrier | 4 | — | — | 4 |
| Clinical diphtheria: positive swab. Not admitted | — | — | 7 | 7 |
| Swab positive: no clinical record | 1 | 2 | — | 3 |
| Clinical diphtheria: no swab, or swab was negative | 3 | 4 | — | 7 |
| Total | 28 | 13 | 7 | 48 |

The seven cases "not admitted" were children brought to the non-employee clinic; a swab was taken and the parents were told to bring the children the next day. When the parents fail to do this it is virtually impossible to locate the patient. It is fairly easy to find an employee by his personal number, but finding "Ali the son of Mohammed who lived at the house of Yadollah" is an insuperable obstacle.

The seven cases included on clinical grounds were all children between 2 and 4 years, admitted at a late stage of the disease, with extensive membrane formation, toxaemia, cyanosis, and laryngeal obstruction.

The age incidence of Iranian patients is shown in Table III.

TABLE III.—*Incidence of Iranian Patients*

| Age (Years) | Died | Recovered | Carriers | Total |
|---|---|---|---|---|
| 0-2 | 4 | 0 | 0 | 4 |
| 3-5 | 7 | 12 | 0 | 19 |
| 6-20 | 1 | 8 | 1 | 10 |
| Over 20 | 0 | 2 | 2 | 4 |
| Total | 12 | 22 | 3 | 37 |

The four British cases were all adults. Two men, aged 26 and 28, one with a little tonsillar membrane and the other with none, had a mild sore throat with fever. A woman aged 30 was affected equally mildly. All three recovered rapidly. The fourth patient, a woman of 31, was in a desperate condition, with massive membrane formation, respiratory obstruction, "bull-neck," and toxaemia within 24 hours of the onset of symptoms, death occurring ten days later. These four were all mitis infections.

Table III indicates clearly that the disease is most severe below the age of 5. Nearly half the children died, and those who recovered were extremely ill with toxaemia and extensive membrane formation. Delay in obtaining medical attention was evidently largely to blame for the fatalities. Three of the "under 2" group had been ill for three, six, and nine days, and one fatal case in the 3–5 year group had been ill for 10 days. Included also in the latter group are the three fatal "unproved cases," quoted in Table II, which were in such a desperate state that death occurred a few hours after admission. Similarly, the fatal case in the 6–20 age group was that of a boy of 7 who had been ill four days and who on admission was drowsy, vomited repeatedly, and had a liver enlarged three fingerbreadths.

*Concurrent Infections.*—In one case Vincent's organisms were present, in five cases a haemolytic streptococcus, and in two cases both haemolytic streptococcus and Vincent's organisms.

*Other Throat Infections.*—During the period under review the total number of swabs cultured, other than "follow-up" swabs of diphtheria and swabs of contacts, was 805. The positive findings were:

| | |
|---|---|
| *C. diphtheriae* | 41 |
| Haemolytic streptococcus | 191 |
| *Staphylococcus aureus* | 70 |
| Vincent's organisms | 50 |
| Pneumococcus | 11 |
| *Bact. coli* | 9 |
| Pneumobacillus | 2 |
| *Oidium albicans* | 2 |

Acute streptococcal throat seems to be about five times as frequent as diphtheria, and the pneumococcus is notably rare.

## Summary and Conclusions

Forty-eight cases of diphtheria occurring in a large Persian community in Abadan, South Persia, since January, 1948, are described. The incidence of the disease is far less than in European countries, despite a non-immunized community. Infections are predominantly of the mitis type and relatively mild in adults. There is a high mortality rate in children below the age of 5, mainly because of delay in obtaining medical advice, and the need for preventive measures seems to be in infancy rather than in children of school age.

The incidence of other throat infections is recorded, and shows acute streptococcal throats to be about five times as frequent as diphtheria.

We are indebted to Mr. A. C. Turner, O.B.E., chief medical officer of the Anglo-Iranian Oil Company in Iran and Iraq, for permission to publish this paper, and to Professor J. W. McLeod, O.B.E., F.R.S., of the University of Leeds, for criticism and advice.

### REFERENCES

Anderson, J. S., Happold, F. C., McLeod, J. W., and Thomson, J. G. (1931). *J. Path. Bact.*, **34**, 667.
Gordon, M., and Higginbottom, C. (1942). Ibid., **54**, 435.

Discussing the treatment of injured miners underground, the Report of H.M. Chief Inspector of Mines for the year 1948 says: "All that happens, down to the smallest detail, to a seriously injured person in the period immediately following an accident may well determine whether the injury received is to result in least disability or something more than that. If the injured person is fortunate there is (i) a competent first-aid man, (ii) the necessary equipment, and (iii) both of these near at hand. The efforts of those whose responsibility it is to organize first-aid at mines must be directed to establishing and maintaining these components of what has been termed the *Essential Trinity* of an efficient first-aid service. The first-aid equipment available to an injured man depends upon effective distribution. This has been greatly facilitated by the increased use of tubular first-aid containers. Their use has now become more widespread, and one division alone has ordered over a thousand of them. Contributing also to the improvement that has been noticed in the distribution of first-aid equipment has been the adoption by managements of what has come to be known as the '250–1,000–250 yard rule' to govern the distribution of first-aid stations below ground. Its observance requires that there shall be a first-aid station within 250 yards of the shaft bottom, within 250 yards of the face, and at intervals not exceeding 1,000 yards along the main roadways on which men work or travel."

# Medical Memoranda

## Spontaneous Rupture of Bladder Associated with Unusual Congenital Anomalies

In this case a diverticulum of the bladder, which ruptured, was associated with unusual congenital defects. Taylor (1948) reported a case of spontaneous rupture of the bladder and reviewed the literature.

### CASE REPORT

An unmarried garage storekeeper aged 23 was admitted to the Radcliffe Infirmary suffering from severe abdominal pain. The previous day he had had an intermittent pain in the right lower quadrant of the abdomen; he had passed urine normally before retiring. Soon after rising at 7 a.m., feeling perfectly well, he passed urine normally and had a normal bowel action. He was then immediately seized by a sudden violent pain in the hypogastrium, which spread over the entire abdomen. He did not vomit. Four months previously he had had a similar but less severe attack which lasted only half an hour. He had never had any difficulty in micturating, and considered his stream of urine satisfactory. He had been operated on for hare-lip while an infant, and his hands and feet had always been deformed. He had had blepharitis for years and otitis media as a child: there was no other relevant personal or family history.

On examination his temperature was 98° F. (36.7° C.) and pulse 96. He appeared shocked; his tongue was furred and his breath foul. There was generalized abdominal rigidity and recoil tenderness, and the pelvic peritoneum was tender on rectal examination. There was hyperaesthesia in the right iliac fossa, and tenderness seemed to be maximal in this area. There was no obvious abnormality in the nervous system. A diagnosis was made of general peritonitis due to a perforated appendix, and an intravenous saline drip was started.

*Operation.*—Seven hours after the onset of the pain the abdomen was opened under general anaesthesia by a right iliac muscle-split incision. Over a pint (570 ml.) of urine was sucked from the peritoneal cavity. The bladder was felt to be distended, and a thin-walled diverticulum bulging from its superior surface on the right side was seen to be leaking urine. This bullous sac measured some 7.5 by 10 cm. and had a thin, bluish, translucent wall apparently consisting for the most part of mucous membrane only; the small rupture, less than 1 cm. across, was clamped off. A right paramedian incision was made. The bladder still contained about 500 ml. of urine. The right ureter was 3 cm. in diameter, but the left was not clearly seen. The diverticulum was now excised: it opened into the bladder by a wide mouth, and had no real neck. The interior of the bladder appeared to be normal, but the external urinary meatus was the size of a pin-hole, and there was a glandular hypospadias. After dilatation an indwelling urethral catheter was passed. The bladder was closed with two layers of catgut around a small rubber tube through a separate suprapubic stab incision. The peritoneum was closed over the bladder, and the wound was closed in layers.

*Pathological Report.*—The specimen consisted of a flattened ovoid diverticulum (9 by 6 cm.) with a wall almost constantly 0.2 cm. in thickness. All sections of the diverticulum examined were lined throughout by squamous epithelium, with varying degrees of keratinization. No transitional epithelium was seen. The squamous layer was flattened and did not show the degree of irregularity usually seen after metaplasia. The wall consisted of fibrous tissue showing scanty diffuse round-cell infiltration, much less than might be expected in a bladder when extensive squamous metaplasia had occurred. In the fibrous layer were widely separated small bundles of smooth muscle fibres, but there was no evidence of a complete muscular coat.

Convalescence was protracted by a urinary-tract infection (culture: *Pseudomonas pyocyanea*) and a persistent residual urine, but three months after operation the patient was in good health and his stream was satisfactory. He still had some frequency of micturition, however, and his urine contained pus cells and grew *Ps. pyocyanea* on culture. An intravenous pyelogram two weeks after operation showed good concentration of the dye on both sides and some degree of dilatation of both renal tracts, especially the right.

*Congenital Anomalies.*—These added interest to the case. A complete cleft palate and hare-lip were operated on when the patient was 14 weeks old; the premaxilla was excised and the hare-lip sutured. The hands showed two most unusual anomalies (Fig. 1). The index finger of the right hand was fused with the thumb, the first phalanx crossing the thenar space (Figs. 2 and 3). In the left hand the first phalanges of the ring and middle fingers united to articulate in true syndactyly with a single second phalanx (Fig. 4). The ring and middle fingers of the right hand were webbed together in zygodactyly, and showed a flexion contracture, and the left index finger did not extend beyond its first phalanx. In both hands there was an abortive attempt to form a further finger at the head of the second metacarpal. The feet also showed zygodactyly and an extra bone at the head of the second metatarsal. The patient did not wish for any plastic or reconstructive surgery. Where congenital anomalies are found there is usually a relevant family history, but none could be obtained in the present case.

FIG. 2.—Right hand in use, showing index finger fused with thumb.

FIG. 1.—Dorsal view of both hands.

FIG. 3.—Radiograph of right hand.

FIG. 4.—Radiograph of left hand.

### COMMENT

Spontaneous rupture of a diverticulum of the bladder was noted in three cases quoted by Lipow and Vogel (1942). The remarkable features in the present case were the absence of history, signs, or symptoms incriminating the urinary system, and the associated congenital anomalies. The usual feature of vomiting was also absent. The only identified cause of obstruction was the pin-hole meatus, and it seems that this was the cause of the urinary obstruction. Chronic distension of the bladder, a diverticulum which eventually ruptured under the strain of defaecation, and bilateral infected hydronephroses followed.

I am indebted to Mr. A. Elliot-Smith for permission to publish this case, to Dr. R. H. Cowdell for the pathological report, to Dr. F. H. Kemp for the radiographs, and to Mr. E. L. P. Tugwell for the photographs.

NEIL WARD-MCQUAID, M.B., F.R.C.S.,
Surgical Tutor, Radcliffe Infirmary, Oxford.

### REFERENCES

Lipow, E. G., and Vogel, J. (1942). *J. Urol.*, **47**, 277.
Taylor, R. A. R. (1948). *Brit. J. Urol.*, **20**, 117.

## Fatal Air Embolism Due to Vaginal Douching in Pregnancy

It would be interesting to know how general is the knowledge, among both practitioners and gynaecologists, that vaginal douching and insufflation during pregnancy may be a dangerous procedure.

Forbes (1944) reviewed the causes of air embolism in general, described a case of his own, and mentioned fatalities during therapeutic vaginal insufflation recorded by Peirce (1936), Latham Brown (1943), and Partridge (1943).

Brown's case was that of a primipara aged 25 who had been douched and insufflated in the sixth and seventh months of pregnancy and who died within a few minutes of the start of a further insufflation seven days before her expected date of delivery. At necropsy, the cervix was drawn up and dilated to two fingers; the edge of the placenta was stripped about 1 in. (2.5 cm.) deep, the membranes were completely free on that side, and there had been slight haemorrhage; in the heart, the right ventricle contained large bubbles but very little blood.

Partridge gave the warning that air insufflation of the vagina near term is a very dangerous procedure. His case was that of a 1-para aged 21. Two days before her expected delivery she was insufflated with "picrotal" for trichomonas; after about 10 pumps the insufflator was withdrawn; then the patient had a convulsion, became cyanosed, dyspnoeic, and died in about three minutes. At necropsy frothy blood was found in the right heart, and air in the veins of the neck, the cerebral sinuses, and the pampiniform plexus; the cervix was large, patulous, and eroded; there was no evidence of bleeding, or of separation of the placenta or membranes. The placenta was placed high and "air was found on its maternal surface."

Forbes (1944) considered his case to be the first in which simple vaginal douching led to air embolism from detachment of the placenta. A woman of 34, with three previous pregnancies, started an apparently normal period on July 1, 1943. The next night she collapsed on her way to bed and died soon after. At necropsy, 17 hours later, Forbes found a blood-stained pad between her legs, an open cervical canal with an erosion round the external os, "no injury," but the placenta placed low and with its lower edge detached to a depth of 1 in., and the membranes separated to a depth of 2½ in. (6.3 cm.); a 3-months foetus in intact membranes; fine froth in the trachea; oedematous lungs; and the right chambers of the heart dilated and filled with frothy blood. Microscopically, there were numerous small infarcts in the lungs. Forbes was doubtful whether even the woman knew that she was pregnant, but as she was accustomed to using a Higginson syringe to douche her vagina, he thought it fairly certain that she had done so on this occasion and accidentally killed herself.

Benjamin (1946) reported the case of a girl aged 17, about five months pregnant, who died shortly after her paramour had blown strongly from his mouth into her vagina. In the absence of a demonstrable *corpus delicti* the man was released by the court.

Breyfogle (1945) reported the case of a 3-gravida aged 21 who was insufflated with silver picrate compound for vaginal discharge when seven months pregnant; symptoms of collapse did not start until five minutes after insufflation had been completed, and she died within 30 minutes. She had been insufflated also in the fifth month. Breyfogle found frothy blood in the right heart but not elsewhere. The placenta and membranes were intact. He thought that at least 500 c.cm. of air must have been forced into the pregnant uterus. After writing his paper he noted the report of another fatal case following insufflation in pregnancy (*Amer. J. Surg.*, 1945, **130**, 164).

The following case occurred recently.

### CASE REPORT

The patient, aged 35, had had four previous pregnancies, including twins 1 year old. Her last period was towards the end of April, 1949, but she had been very irregular before that. On the night of June 29 she prepared to have a bath before going to bed, and was found at 10.15 p.m. collapsed on the bathroom floor, with a Higginson syringe lying between her legs; she was alive, but could not speak, and died shortly after. At necropsy 13 hours later a few drops of fluid were found just inside the vagina; this fluid contained traces of soap, similar to the teaspoonful of fluid that remained in the Higginson syringe.

A 49-mm.-long foetus was found in an intact and apparently undisturbed uterus; the cervical canal contained a mucous plug, the external os showed a complete delicate pink ring of erosion, and there was no sign of the slightest haemorrhage. On cutting the uterine wall in several places the blood which escaped was frothy.

When examined *in situ* the right ventricle of the heart was almost distended by finely frothed blood. Apart from generalized left pleural adhesions and congestion of both lungs, there was no other clear abnormality in the body.

A report was sent to the coroner that death had been due to air embolism from the use of a Higginson syringe, and that even if deceased knew that she was pregnant (which was doubtful), she might have been merely douching herself for hygienic purposes.

Thanks are due to Mr. Norman Graham, the coroner, for permission to report the case.

R. T. COOKE, M.D.

### REFERENCES

Benjamin, H. (1946). *J. clin. Psychopath.*, **7**, 815.
Breyfogle, H. S. (1945). *J. Amer. med. Ass.*, **129**, 342.
Brown, R. L. (1943). *Lancet*, **1**, 616.
Forbes, G. (1944). *British Medical Journal*, **2**, 529.
Partridge, A. J. (1943). Ibid., **2**, 329.
Peirce, S. J. S. (1936). *Canad. med. Ass. J.*, **35**, 668.

Information about nursing as a career is being given at the Schoolgirls' Exhibition at the New Horticultural Hall, London, S.W.1. There are displays from ten hospital groups and two regional hospital boards, with demonstrations of the nurse's work and training. Nursery nursing is demonstrated, and also mothercraft training. The exhibition will close on June 3.

# Reviews

## THE ACUTE APPENDIX

*Acute Appendicitis and its Complications.* By Frederick Fitzherbert Boyce, M.D. Oxford Medical Publications. (Pp. 487; illustrated. £3 10s.) London: Geoffrey Cumberlege. 1949.

From time to time it is salutary to review our knowledge of well-worn subjects, and this book on acute appendicitis comes opportunely to remind us that our present learning is little in advance of what Fitz taught us in 1886. The reader will find in it an excellent compendium of the many opinions which have been, and still are, held on the causation, diagnosis, and treatment of this deadly complaint. The author is very fair in his judgments—perhaps too fair, for his opinion is so balanced that in some places we hardly know what his own views are.

The theme of the book is the *urgency* of acute appendicitis, and stress is laid on the variability of the symptoms. The author is critical of the dogmatic teaching of some authorities. For example, he writes: "It is not true, as Moynihan stated, that if pain be not the first symptom, then the disease is not appendicitis." Certainly there are exceptions, but students should be taught the rule; long experience tells that it is as likely that the history-taker will be at fault as that abdominal pain will not be the first symptom.

There is a long section on the causation of appendicitis, but little new light is thrown on the subject. Almost a page is given to a consideration of the views put forward in the correspondence columns of the *Journal* in 1940, and the statement is made: "The fact that such a discussion could take place in the columns of a highly respected medical journal in the year 1940 is as good an indication as any of the still unsettled aetiology of acute appendicitis."

Many of the author's conclusions are based on a survey of over 6,000 cases treated during fifteen years at the Charity Hospital of Louisiana at New Orleans. Significant reference is made to the remarkable fall in the mortality of appendicular peritonitis in the City of Philadelphia after the crusade originated by Bower. It is to be noted, however, that while Bower attributed the improvement to the greater use of the conservative method of treatment the author assigns it to other causes. Surely this important question ought to be decided by an impartial re-examination of the data. This is a stimulating book which should be referred to by all surgeons and practitioners; it is perhaps not quite dogmatic enough for students. There is a good bibliography, but I was surprised not to see therein A. J. Ochsner's *Handbook of Appendicitis.*

V. ZACHARY COPE.

## TOPICAL THERAPY

*Current Therapy. 1950.* Edited by Howard F. Conn, M.D., and twelve consulting editors. (Pp. 736. £2 10s.) Philadelphia and London: W. B. Saunders Company.

This handsome volume has the same purpose as the 1949 edition—bringing to the practising physician authoritative information on the latest approved methods for the treatment of disease. It differs from the "recent advances" type of book in that it is designed to be comprehensive in itself and to contain all—not merely the most recent—therapeutic information that the busy doctor needs. When variations in standard therapy exist, two or even more methods of treating a single disorder are sometimes included; no preference is indicated among such variant methods.

The work is produced by 260 contributors, representing many of the foremost clinicians in the United States, working under a board of twelve distinguished editors with a presiding editorial genius. This type of book, representing a large number of abstracts of therapeutic information, is popular in the United States just now, and follows a somewhat similar large volume recently reviewed in the *Journal.* The work is of great value to the busy practitioner or consultant anxious to recall a drug or to verify a dose, or to refresh his memory on some current method of treatment without the necessity of much reading. It contains a remarkable amount of accurate, up-to-date, and concise information. Its value in this country may be limited by the unfamiliarity of the names of some of the recommended drugs, and many of the foods in the diets prescribed are not only unfamiliar but unobtainable here. On the whole, however, it is encouraging and gratifying to see how closely therapeutic practice in the U.S.A. and in this country conform, though it is almost inevitable that the reviewer of such a large work should occasionally find himself in disagreement with some of the measures advocated. This is definitely a work of reference and not one for the undergraduate, whose therapeutic knowledge should as far as possible be based on the inculcation of principles and not derived from an attempt to memorize a mass of tabulated factual information.

D. M. DUNLOP.

## RECTAL SURGERY

*Anus, Rectum, Sigmoid Colon.* By H. E. Bacon, M.D., F.A.C.S. Third edition. Volumes 1 and 2. (Pp. 1,127; profusely illustrated. £11 the set.) Philadelphia and London: J. B. Lippincott Company.

The third edition of this well-known textbook on the anus, rectum, and sigmoid colon is in two large volumes, which are profusely illustrated in colour and black-and-white. Each chapter is an authoritative and impartial exposition of its subject. Chapter 19, on malignant disease, which runs to no fewer than 250 pages and has over 1,100 references, is a remarkable achievement. The Babcock–Bacon pull-through operation of proctosigmoidectomy is fully described and illustrated; the other surgical methods, such as anterior resection and radical combined excision, are also described and their relative advantages and indications set out fairly. Equally important are the final chapters on anaesthesia, pre- and post-operative treatment, and the uses of alloy steel wire in surgery. The complete references at the end of each of the twenty-nine chapters are a major contribution to making this a work of first-class importance. There is no doubt that this is the largest, the most up-to-date, and the most complete work on proctology in the English language. The printing and illustrations are superlative, and no praise is too great to the author, his assistants, and the publishers for having brought this great standard work to completion.

W. B. GABRIEL.

## SURGICAL TREATMENT OF HYPERTENSION

*Traitement Chirurgical de l'Hypertension Artérielle.* By Maurice Luzuy and Jean F. Porge. With 58 figures by H. K. Wagner. (Pp. 160. 500 francs.) Paris: G. Doin. 1948.

This monograph on the surgical treatment of arterial hypertension is a review by French observers of the operative methods employed in the treatment of hypertension in the

United States. It includes also a full consideration of the pathology, symptomatology, and classification of hypertensive disease. The language is crystal clear; the beauty of its diction makes it a joy to read and is a striking reminder of the suitability of the French language as a vehicle for scientific communication.

The authors' approach to the problem of hypertension affords a valuable comparison between medical science in France and in the U.S.A. They tacitly assume original inspiration and critical analysis to be the attributes of the French medical scientist, while agreeing that large-scale assessment of a long series of cases is more typically an American than a European exercise. American and English readers, while admiring the shrewdness and logic of the arguments set forth and the presentation of anatomical and physiological detail and diagram, might suggest that too large a body of theory had been built up, albeit logically, on a rather slender basis of observation; they might miss the record of a personal clinical experience as manifest in statistical analysis of a long series of clinical cases. Statistical analyses are provided, but are in nearly all cases reproduced from American sources.

The chief virtue of the work lies in its full historical account of the attack on hypertension from its European beginnings to its American fruition. It is notable that at the head of the introduction is the typically dramatic statement of Professor Leriche: "To reduce the number of hemiplegias, what a fine surgical adventure!" It is also to be recommended for the detailed anatomical description of the various operative procedures available and the excellent diagrams of M. Wagner.

The investigation of the patient before operation is undertaken is very fully considered; the ophthalmoscopic signs are presented in unusual detail. The book is a most valuable collection of data on the clinical aspects of hypertension not readily accessible elsewhere, and the French in which it is written is easy to read.

IAN AIRD.

## MANAGEMENT OF OBESITY

*Obesity.* By Edward H. Rynearson, M.D., F.A.C.P., and Clifford F. Gastineau, M.D. (Pp. 134. 17s. 6d.) Oxford: Blackwell Scientific Publications.

This excellent little book follows conventional lines in its review of the cause and treatment of obesity. The authors draw attention to the hazards which beset the adipose, stress the simple physiological basis of the condition, and discuss the possible aetiological factors. In conformity with current American views, psychological aspects of overeating are given pride of place.

A full account of dietetic management follows. It must be admitted that the details will be of more value to the American reader than to the English, whose table is seldom adorned by lean sliced ham, water-packed peaches, summer squash, rutabagas, and cooked hominy. Nevertheless, the principles hold good on both sides of the Atlantic. The book closes with some remarks on psychotherapy and the use of drugs. An aggressive approach is recommended; the patient should be shown tables to illustrate the effect of obesity on mortality, and told that he is "digging his own grave with his teeth." Indiscriminate thyroid medication is rightly condemned, but no final decision is reached on D-amphetamine. This is a useful straightforward account of a condition which is perhaps taken more seriously in the United States than in the United Kingdom.

R. BODLEY SCOTT.

## BOOKS RECEIVED

*Review is not precluded by notice here of books recently received*

*The Principles and Practices of Rehabilitation.* By H. H. Kessler, M.D., Ph.D., and others. (Pp. 448. 63s.) London: Henry Kimpton. 1950.

*Clinical Radiation Therapy.* Edited by E. A. Pohle, M.D., Ph.D., F.A.C.R. (Pp. 902. 105s.) London: Henry Kimpton. 1950.

*The Atlantic Civilization: Eighteenth-Century Origins.* By M. Kraus. (Pp. 334. 30s.) London: Geoffrey Cumberlege. 1949.

*Combined Textbook of Obstetrics and Gynaecology.* Edited by D. Baird, D.P.H., F.R.C.O.G. 5th ed. (Pp. 1,411. 70s., plus 1s. 3d.) Edinburgh: E. and S. Livingstone. 1950.

*Sexual Behaviour in Society.* By A. Comfort, M.B. (Pp. 158. 8s. 6d.) London: Gerald Duckworth. 1950.

*Some Relations between Chemistry and Biology.* By Sir C. N. Hinshelwood, F.R.S. (Pp. 14. 2s.) Oxford: Blackwell. 1950.

*Royal National Hospital for Rheumatic Diseases, Bath. Reports. Vol. 3. 1948-1949.* (Pp. 284. No price.) Bath: Royal National Hospital for Rheumatic Diseases. 1950.

*Practical Procedures in Clinical Medicine.* By R. I. S. Bayliss, M.D., M.R.C.P. (Pp. 445. 25s.) London: Churchill. 1950.

*A Short Textbook of Radiotherapy.* By J. Walter, M.R.C.P., D.M.R.E., and H. Miller, M.A., Ph.D. Foreword by J. L. A. Grout, M.C., F.R.C.S.Ed., D.M.R.E. (Pp. 444. 28s.) London: Churchill. 1950.

*Medical Entomology.* By R. Matheson. 2nd ed. (Pp. 612. 54s.) London: Constable. 1950.

*A New Approach to the Treatment of Burns and Scalds.* By L. Colebrook, F.R.S., F.R.C.O.G. (Pp. 174. 12s. 6d.) London: Fine Technical Publications. 1950.

*Digitalis and other Cardiotonic Drugs.* By E. R. Movitt, M.D. 2nd ed. (Pp. 245. 45s.) New York: Oxford University Press. London: Geoffrey Cumberlege. 1949.

*Some Contemporary Thinking about the Exceptional Child.* (Pp. 64. No price.) Langhorne, Pa.: The Woods Schools. 1949.

*Physicians' and Nurses' Concise Medical Encyclopaedia.* By W. H. Kupper, M.D. (Pp. 450. $7.50.) Los Angeles, Cal.: Biblion Press. 1950.

*Handbook of Obstetrics and Diagnostic Gynecology.* By L. Doyle, M.S., M.D. (Pp. 240. $2.) Palo Alto, Cal.: University Medical Publishers. 1950.

*Autosuggestieve Psychotherapie.* By B. Stokvis. (Pp. 137. 8.95 francs.) Lochem: De Tijdstroom. 1950.

*Aspetti Medico-Sociali della Mortalità Infantile.* By G. B. Allaria. (Pp. 115. No price.) Rome: Istituto di Medicina Sociale. 1950.

*Saggi Diagnostico-Terapeutici di Medicina Interna.* By D. Campanacci. (Pp. 294. 1,500 lire.) Turin: Minerva Medica. 1949.

*Die Einteilung des Nervensystems nach seinen Leistungen.* By L. R. Muller. 2nd ed. (Pp. 74. M. 8.70.) Stuttgart: Georg Thieme. 1950.

*Klinische Pathologie der Blutkrankheiten.* By R. Schoen and W. Tischendorf. (Pp. 521. M. 57.) Stuttgart: Georg Thieme. 1950.

*Spezielle Therapie der Herz- und Gefässkrankheiten.* By I. Zárday. (Pp. 188. No price.) Dresden and Leipzig: Theodor Steinkopff. 1948.

*Die Liquordiagnostik in Klinik und Praxis.* By H. Demme. (Pp. 212. M. 16.) Second edition. Berlin: Urban and Schwarzenberg. 1950.

BRITISH MEDICAL JOURNAL

LONDON

SATURDAY MAY 27 1950

## THE TRAINING OF THE G.P.

It is apparent from the letters recently published under the heading "The G.P. at the Crossroads" that general practitioners are concerned about the difficulty of maintaining a high standard of work in the National Health Service. The report,[1] published to-day and summarized on another page, of the B.M.A. Committee which has been considering the postgraduate education of general practitioners will therefore be read with special interest, and the chairman, Sir Henry Cohen, and members of the Committee may be certain of receiving the thanks of the profession for compiling the necessary sequel to the report[2] on undergraduate education which appeared two years ago. Unlike some sequels, the present report equals in interest and value the document which preceded it. After nearly two years of the National Health Service it has become increasingly clear that general practice has suffered and hospitals have benefited, at least financially, from the new regime. None can deny that the public will best be served by having a strong general-practitioner service, backed up by well-equipped hospitals. The present disparity between the development of general practice and hospitals is ultimately to the detriment of both. General practitioners have lost work which should be done by them, and hospitals have been burdened beyond their capacity.

Although the system of remuneration which has been adopted in the N.H.S. has been an important cause of the changing face of medicine, nevertheless it is within the power of the profession to counter the adverse forces by raising the professional status of general practice. The Committee came to the conclusion that the character and scope of general practice entitle it to rank as a special branch of clinical work, and that the personal and professional qualities demanded of a general practitioner are no less than those demanded of many specialists. They suggest that for the attainment and maintenance of a high standard of general practice a period of systematic postgraduate preparation for practice and opportunity for continued education throughout the period of active practice are required. The suggested postgraduate training for general practice is to occupy three years after registration. The first year will consist in training under the supervision of a general practitioner. During the second year there will be special training in posts, preferably residential, in district hospitals under regional hospital boards. A choice of opportunities is suggested for the third year, including senior training appointments in hospital departments for varying periods of one to three months, simultaneous clinical assistantships in different subjects, further assistantships in general practice, or locum appointments in approved general practice for a total period not exceeding three months. Although the postgraduate training would be given largely outside teaching hospitals, it is thought desirable that it should be organized and supervised by an academic body and that universities or medical schools should appoint a dean of postgraduate education. Proposals such as these will inevitably cause argument, and there may be disagreement about the allocation of work within the training period, if the important principle of a lengthy training is accepted. Before the war many newly qualified doctors went directly into general practice, but one-year house appointments are to be compulsory under the new Medical Bill. Any experience of hospital work helps to ease the difficulties encountered by those entering general practice: nevertheless, an additional year in hospital would certainly assist the embryo practitioner to add to his knowledge, particularly in such specialties as dermatology, otolaryngology, and anaesthetics. It is not at all unusual to find men in general practice to-day who have had more than two years' hospital experience.

The administrative separation of the regional boards and the general-practitioner service has led to difficulties, and the proposal that general practitioners should have special training in hospital underlines the need for integration—a need felt by the patient. The present-day district hospital and the hospital of the future cannot function efficiently without a number of registrars and senior registrars to assist with the great and ever-growing volume of out-patient work and with the increasing complexity of medical therapy. Reducing the mortality and morbidity of vascular thrombosis, haematemesis, and acute uraemia, for example, make heavy demands on the medical staff. It is becoming clear that in the future the number of registrar appointments, except those in the senior grade, cannot be equated with vacancies for consultants, and many registrars will therefore become general practitioners. There is here a common need between the hospitals and the general-practitioner service which should be worked out in detail. In an interim report on the relationship between general practitioners and the hospital and specialist services a joint

[1] *General Practice and the Training of the General Practitioner*, 1950. Published by the British Medical Association. Price 7s. 6d.
[2] *The Training of a Doctor*, 1948. Published by the British Medical Association.
[3] Interim Report of Health Centre Committee, 1948.

subcommittee of the General Medical Services Subcommittee (Scotland) and the Central Consultants and Specialists Committee (Scotland) has pointed out the danger of hospitals having to increase their junior staff in order to treat the growing numbers of out-patients not requiring specialist attention. Widening the lower rungs of the specialist ladder will mean more "casualties" in the scramble for specialist appointments, and much harm would be done to the status of general practice if recruits had mainly to be sought among these casualties. It would be undesirable to have two grades of junior registrar, but it should be entirely feasible to organize the work of registrars so that part of their time could be spent in work of special value to them if they later entered general practice. Such an arrangement would appreciably assist towards establishing a closer working liaison between practitioner and hospital, for the practitioner would then be well aware of the potentialities of the hospital service and of its difficulties—for example, in relation to the chronic sick. A valid criticism of medicine to-day is the relative lack of contact between general practitioners and the hospital staff. Domiciliary consultations have certainly increased the opportunities of mutual discussion of common problems, but there is still insufficient encouragement given to practitioners to mingle with their colleagues in the hospital. A brief discussion over, for example, a patient with an anxiety state may be of greater assistance to the practitioner in his subsequent care of the patient than a possibly belated letter from the hospital. Perhaps some hospitals might find it possible to allow general practitioners to have meals with medical staff and thus to increase the opportunity for social and professional contact, for which, as Sir Henry Cohen's Committee points out, there is great need.

The suggestion that the trainee assistant should pass from his internship to general practice and then return a year later to do hospital work will probably be criticized. It may, indeed, be preferable for the budding practitioner to acquire his experience in medical techniques as a junior registrar in hospital before beginning in supervised practice. Consultants will acknowledge, if only after the port, their own continued education from their registrars in recent advances—for example, in modern electrocardiograms. The experienced general practitioner will be of the greatest help in introducing general practice to novices, but the initiates in their own turn can contribute towards the postgraduate training of their principals. Besides emphasizing that the general practitioner must not be isolated either from other medical services or from his colleagues, the Committee recommends that he should have easy access to diagnostic facilities and ancillary services, such as physiotherapy. The organization of practice is discussed only in so far as it has a bearing on postgraduate education. Health centres were discussed in the Association's interim report[3] published in 1948, and the Cohen Committee did not return to this subject. There is no doubt that the well-organized health centre would provide practitioners not only with opportunities for meeting their professional colleagues but also with the leisure to maintain themselves as cultured and informed members of the community. Until health centres can be built, more might be done towards the grouping of practices and arranging of rotas of duty. Hospitals should attempt to meet the needs of practitioners for laboratory investigations even if only to a limited extent. The well-trained practitioner will have earned the right to direct laboratory investigation of his patients and will have learnt to differentiate those who really need the advice of the hospital consultant. The report gives an encouraging account of the nature, scope, and future of general practice, and in itself will surely stimulate the interest of many holding junior hospital posts to-day. The chairman of the Committee has clearly taken a hand in the compilation of the report, which is as easy to read as it is informative. The Committee believes that the fulfilment of its recommendations will ease the lot of the general practitioner by raising his status in the eyes of the profession and the public, by stimulating his interest in the progress of the art and science of medicine, and by providing him with the means of maintaining and refreshing his knowledge and skill, and so of pursuing his practice with the pleasure and satisfaction which come from efficiency. Its aim is, in short, to give him the opportunity of becoming what Osler called "that flower of the profession—the cultivated general practitioner."

## STREPTOMYCIN RESISTANCE OF TUBERCLE BACILLI

The resistance of some tubercle bacilli to the action of streptomycin has been the most serious difficulty encountered in the treatment of pulmonary tuberculosis with this drug. There is evidence that bacterial strains resistant to chemotherapeutic agents arise as the result of mutations. These mutations occur in the absence of the drug, but the effect of giving it is that those organisms which are resistant to it survive, while the others do not. Thus in cases of pulmonary tuberculosis treated with streptomycin the sensitive organisms are gradually eliminated and the resistant ones multiply. This obstacle in streptomycin treatment was recognized in the Medical Research Council's report[1] which was

[1] *British Medical Journal*, 1948, **2**, 769.
[2] *Amer. Rev. Tuberc.*, 1949, **59**, 438.
*Lancet*, 1949, **2**, 1237.
[4] *Amer. Rev. Tuberc.*, 1950, **61**, 483.
[5] *Lancet*, 1950, **1**, 878.

published in this *Journal* in 1948. Streptomycin resistance was studied in 41 cases, and strains of tubercle bacilli with a degree of streptomycin resistance more than 10 times that of a control were found in 35 cases, usually within the first two months of treatment. It was accordingly decided to attempt to alter the development of streptomycin resistance by the use of various schemes of dosage. The report to the Streptomycin in Tuberculosis Committee of the Medical Research Council which is published in this issue is the account of this attempt.

Four schemes of dosage were used. In the first a group of nine patients was treated with 0.5 g. of streptomycin six-hourly for alternate weeks; in the second, 13 patients were given 0.5 g. of streptomycin six-hourly for alternate months; the third group of 12 cases had 0.25 g. of streptomycin six-hourly without intermission; and the fourth group of 11 cases had 1 g. of streptomycin in one dose daily without intermission. The cases admitted to the trial were of the same general type as those included in the first Medical Research Council series—that is, cases of acute progressive bilateral pulmonary tuberculosis of presumably recent origin, unsuitable for collapse therapy, the patients being between 15 and 30 years of age. Treatment was continued for six months, and the time in the course when streptomycin-resistant organisms were isolated from sputum was noted for each case and the results in the different groups compared. In analysing the results a degree of resistance eight times or more that of the control strain was regarded as significant. The emergence of streptomycin-resistant bacilli in all the groups occurred at approximately the same time and in the same proportion of cases in each group. Also, the degree of streptomycin resistance was of the same order in each group. So far as this experiment was an attempt to delay the emergence of streptomycin resistance it was, therefore, a failure; but the negative finding is important, and much additional information was obtained.

The groups were reviewed from the point of view of radiographic and clinical change during the period of treatment. There was no significant difference between them, and the single injection of 1 g. daily seemed as satisfactory as the more elaborate methods. The possibility of obtaining information about the development of streptomycin resistance by routine examination of the sputum was also investigated. Specimens of sputum were graded according to their "degree of positivity," and it was found that in most cases this fell in the early stages of streptomycin treatment. When this fall was absent or slight there was a strong tendency to develop a high degree of streptomycin resistance. After the initial fall a later rise in the degree of positivity usually occurred unless the sputum became permanently free from bacilli. When this rise was persistent streptomycin-resistant strains could usually be isolated. Since the bacteriological test used for the determination of streptomycin resistance takes eight weeks, this observation may be of some value to clinicians.

Since this trial ended it has become clear that the most promising work on the possibility of delaying the emergence of streptomycin resistance is concerned with the use of other drugs with streptomycin. Thus the report by Karlson and his colleagues[2] and the preliminary statement by the Medical Research Council[3] suggest that the use of *p*-aminosalicylic acid concurrently with streptomycin may reduce the incidence of streptomycin-resistant strains of tubercle bacilli. The idea of combined drug therapy is not new, and it has been used in other infective processes; but it has not been developed in tuberculosis, because until recently there have been few drugs of any value in this disease. Yegian and Vanderlinde[4] have recently examined in general terms the prospects of combined drug therapy. They point out that, although theoretically possible, in practice it may be difficult to produce a bacterial variant resistant to both of two therapeutically effective drugs used together. They discuss possible regimes of combined drug therapy, such as the use of the drugs together from the beginning of drug treatment or the use of one drug for a period and then the addition of the other. Concerning the latter method, they make the comment that "if the second drug is withheld too long the bacterial population may increase and consist chiefly of cells resistant to the drug given initially, and resistance to the second drug may occur as rapidly as if it had been used alone; thus the effectiveness of combined therapy in reducing the incidence of resistant strains will be lost." It is interesting in this connexion that Carstensen and Linde Andersen[5] state that they use *p*-aminosalicylic acid as a routine in the treatment of tuberculosis, and supplement it by short courses of streptomycin when serious complications occur and before surgical procedures. They have found that the combination of streptomycin with *p*-aminosalicylic acid in this way does not prevent the emergence of resistance to the latter drug. So far there have been no reports of the development of strains resistant to both drugs given in combination to patients who have never previously had either.

It seems clear that the exploration of the clinical possibilities of the drug treatment of tuberculosis is only beginning. Much laboratory and clinical work is now being done on the effect of various combinations of drugs on the tubercle bacillus. The full results of the clinical study being carried out by the Medical Research Council into the use of streptomycin and *p*-aminosalicylic acid in pulmonary tuberculosis will be of special interest and importance.

## TOWARDS A POPULATION POLICY

Nearly a year ago we commented in these columns on the newly published report[1] of the Royal Commission on Population which had been set up in 1944. The objects of the Commission were to investigate present population trends in Great Britain and to consider what measures should be taken to influence the future trend. Among the conclusions reached was one that the present average size of family was 6% below that required for the replacement of population. As a consequence of this the stage is set for a fall in the number of young adults and for a steady increase in the number of those over 65, quite apart from what improved care of the old may achieve. The Royal Commission took the view that a replacement size of family is very desirable in Britain at present, and they accepted the opinion of the Biological and Medical Committee that no physiological or biological factor would prevent married couples having larger families to-day if they wished. In the first volume of the Commission's papers[2] the results were published of a large-scale inquiry into the use of birth control in this country, and the conclusion was reached that the fall over the last 50 years in family size was due not to a diminution of reproductive capacity but to deliberate family limitation.

A different aspect of the population problem is reviewed in the fourth volume of the Commission's papers[3] published last week. This consists of reports of the Biological and Medical Committee on reproductive wastage from the time of conception to the end of the first year of extrauterine life and on involuntary childlessness. Reproductive wastage is important, not only from the national viewpoint but also because abortion and stillbirth may greatly affect the health of the individual woman and her subsequent fertility. The extent of induced abortion is unknown, but the frequency of spontaneous abortion is estimated at about 9%, though this figure must unavoidably contain a proportion of criminal abortions. The Committee noted the importance of setting aside an adequate number of hospital beds for women with threatened or inevitable abortion and of the provision of home help during their absence in hospital as factors assisting in the prevention of foetal loss and in the safeguarding of fertility. A still higher standard of obstetric care of better-fed and healthier mothers, particularly in the lower social classes, might be expected further to reduce stillbirths. Similarly, while the falling infant mortality rate is a reflection of general social progress still more infant lives might be saved by improved maternal education, by the encouragement of family planning, and by the extension of child-welfare services, whether through health authority clinics or by the family doctor. It must be said, however, that a reduction in this reproductive wastage, estimated at present as between 15 and 22% of all children conceived, could not be expected to lead to any considerable net gain in population, because the average family size—which has remained comparatively stable at 2.2 children over the past 20 years—is now largely determined by deliberate family limitation.

If, therefore, the decline in population, predicted to start in 1977, is to be checked one fruitful sphere of endeavour lies in the field of involuntary childlessness, both primary and secondary. The incidence of such involuntary infertility is estimated to be between 5 and 8%, while about 4% of married couples are likely to find their family involuntarily restricted to one child and about 5% to two children. Our knowledge of the causes of infertility is inadequate, but one remark of the Committee deserves wide publicity: "Qualitative study of human semen is still in an early stage, and the standards . . . are still unsettled. Men whose semen appeared on examination grossly defective have been known to effect conception." Thus of wives attending one fertility clinic who subsequently became pregnant defective spermatogenesis, which was not treated, had been considered in 16% the major disability of the couple. What then are the prospects of reducing involuntary childlessness? The Committee believes it a reasonable supposition that about 1–1½% of marriages may be involuntarily childless in a remediable way. Since fertility decreases with advancing age, it would be sensible to encourage early marriage—for instance, by financial inducements such as generous tax allowances for children. Efforts should also be made to dispel the ignorance among the public, and perhaps to a degree among their medical advisers, of the importance of coital technique and of knowledge of the fertile period. Childless couples should be encouraged to seek advice early, in the knowledge that most wives will have become pregnant within two years of "uncontracepted" intercourse. The number of special clinics for infertility is increasing, but, as the Committee points out, there is a lack of co-ordination and of a standardized system of records, while the terms of service must be such as to attract suitably qualified workers to these centres. A welcome should be extended to bodies such as the new Society for the Study of Comparative Fertility, whose inaugural meeting takes place in London next month. The further encouragement and development of fertility clinics and of centres of study and research are as essential to the development of a population policy as to the advancement of scientific knowledge in the field of reproduction.

[1] See leading article in the *British Medical Journal*, 1949, 1, 1127.
[2] See leading article in the *British Medical Journal*, 1950, 1, 169.
[3] Papers of the Royal Commission on Population, Vol. IV. *Reports of the Biological and Medical Committee*, 1950, London: H.M.S.O.

## BORNHOLM DISEASE AND THE COXSACKIE VIRUS

After the Danish physician Ejnar Sylvest[1] had described in 1930 an epidemic of myalgia among the inhabitants of some fishing villages on the island of Bornholm, epidemics and sporadic cases of "Bornholm disease" were reported from all parts of the world. From 1930 to 1934 over 10,000 cases were reported from Denmark alone. In 1933 Pickles published an account of some cases he had observed in Yorkshire.[2] Elsewhere in this issue Dr. J. H. S. Hopkins describes observations made over the past two years which suggest that epidemics and sporadic cases of Bornholm disease are quite common in this country. If mild the disease may often be undiagnosed, while if severe it may simulate appendicitis or pleurisy. Chance observation in another field has recently aroused fresh interest in this subject. Since the isolation of the Coxsackie group of viruses in the U.S.A.—a discovery to which we recently referred in a leading article[3]—several laboratory infections have occurred[4] and the similarity of the patients' symptoms to those of Bornholm disease at once gave rise to the speculation that the Coxsackie virus might be the cause of Bornholm disease. This possibility has now been studied by Dr. G. M. Findlay and Miss E. M. Howard, whose paper on the subject is also published in this issue. It cannot be claimed that the new evidence is entirely conclusive, but these workers have been able to isolate a virus closely resembling Coxsackie virus 2 from the blood, stools, and nasal washings of a patient who had developed typical symptoms of Bornholm disease. One of them suffered a laboratory infection proved by a rise of specific antibody, the illness resembling Bornholm disease. In another laboratory infection in this country the evidence was even more convincing, because the worker concerned had not heard of the suggestion that the symptoms of Bornholm disease were to be expected.

Findlay and Howard thereupon obtained sera from 20 patients who had recently been infected in small epidemics of Bornholm disease in this country. In all cases the sera fixed complement in the presence of antigen made from one of the Coxsackie virus strains. Tests were also done on sera from 16 other patients, who, though not involved in epidemics, had recently suffered from an illness suggestive of Bornholm disease. In 14 of these cases the serum fixed complement with the same Coxsackie virus antigen. Negative results were obtained with sera from 26 healthy persons and also from six patients who had recently recovered from illnesses diagnosed as non-paralytic poliomyelitis or as lymphocytic meningitis. Until more is known about the distribution of Coxsackie antibodies in the general population there must remain a doubt about the significance of a positive complement fixation test, unless an actual rise of titre is demonstrated during the course of the disease, as Findlay and Howard were able to do in one of their cases. The finding of antibodies to Coxsackie virus 1 in this country is also suggestive of specificity. The titres recorded are very low both in this country and the U.S.A., and because of the impure antigens necessarily employed this fact, too, gives rise to uncertainty, though the authors report in general terms observations which support the specificity of the reaction.

That Bornholm disease is caused by a virus of the Coxsackie group must therefore be regarded at the present time as an interesting possibility. Other types of epidemic myalgia distinct from Bornholm disease have been described—such as acute myalgia of the neck and shoulders,[5] brachial neuritis appearing in epidemic form,[6] and myalgia following sore throat[7]—and the question naturally arises whether these are caused by other viruses belonging to the Coxsackie group. The first Coxsackie virus was isolated from cases of paralytic poliomyelitis, and at first it was thought that the myositis it caused was responsible for the paralysis. Recently the correctness of this inference has been doubted, because the Coxsackie virus is frequently isolated from the faeces of patients who are also excreting poliomyelitis virus. Even when the Coxsackie virus only can be isolated from a patient with frank paralysis failure to isolate the poliomyelitis virus may have been due to the technical difficulties of the process. The Coxsackie virus is easy to isolate and the poliomyelitis virus very difficult. Coxsackie virus has also been isolated from patients suffering from illnesses diagnosed as non-paralytic poliomyelitis. This is a very ill-defined syndrome, which might easily be confused with a number of other diseases, including Bornholm disease. Since poliomyelitis and Bornholm disease have a similar seasonal distribution it is not surprising that patients may be excreting both viruses, but then it becomes far from easy to decide which virus is responsible for the patient's illness. An antibody rise during the course of the disease would be important evidence, but antibody develops with great rapidity in Coxsackie virus infections and also in typical Bornholm disease. To demonstrate a rise of poliomyelitis antibody is a most difficult technical feat, even when the infecting strain happens to be of the type which is adaptable to rodents. Moreover, the possibility of double infection cannot be wholly discounted. Fortunately, as Dr. Hopkins points out, the diagnosis in a typical case of Bornholm disease should offer no difficulty.

[1] *Ugeskr. Laeg.*, 1930, **92**, 790 and 982.
[2] *British Medical Journal*, 1933, **2**, 817.
[3] Ibid., 1950, **1**, 233.
[4] Curnen, E. C., Shaw, E. W., and Melnick, J. L., *J. Amer. med. Ass.*, 1949, **141** 894.
[5] Beeson, P., and Scott, T. F. McNair, *Proc. R. Soc. Med.*, 1941-2, **35**, 733.
[6] Wyburn-Mason, R., *Lancet*, 1941, **2**, 662.
[7] Massell, B. F., and Solomon, P., *New Engl. J. Med.*, 1935, **213**, 399.

## TESTING THE RESPONSES OF THE PITUITARY-ADRENAL SYSTEM

In a review of the methods which can be used to detect variations of adrenocortical activity Prunty[1] has emphasized the importance of the relationship between the pituitary–adrenocortical system and certain cellular responses by the organism. Study of the effects of external conditions upon this endocrine system is greatly facilitated by the ease with which the blood eosinophils may be counted. Applying this technique, Roche and his co-workers[2] in Thorn's laboratory have been able to demonstrate the effects of major surgery. In normal conditions there is a sharp fall in eosinophils—indicating increased activity of the system—in the 24 hours after operation. This is followed by a return to supernormal levels after three days. The absence of a sustained fall in eosinophils beyond 48 hours is difficult to understand in view of previous observations on continued high rates of excretion of glucocorticoids for several days after major operations. Workers at the Mayo Clinic, investigating the prolonged effects of cortisone and A.C.T.H., observed that cortisone in contrast to A.C.T.H. affected eosinophils hardly at all.[3] The adrenocortical response to another type of "stress"—namely, anoxia—is well known in animals. Using the eosinophil as a guide, Penneys and his colleagues[4] observed the same response in human subjects after short periods of anoxia.

It is not yet clear what part adrenaline plays in stimulating the anterior pituitary to respond in this way. Workers in Thorn's laboratory have suggested that adrenaline stimulates the adrenal cortex to activity almost entirely through the mediation of the hypothalamus or anterior pituitary.[5] Some of their observations make this difficult to understand, particularly that a dose of 1.5 mg. of adrenaline given to a patient with Addison's disease caused eosinopenia, whereas 100 mg. of A.C.T.H. failed to do so. The explanation they give—that the effect is due to the presence of some functional adrenal tissue—seems to require confirmation.

This same type of difficulty has also been encountered by Spiers and Myer[6] in the course of a careful study of the effects of various conditions on the eosinophils in mice. They observed some decrease in the eosinophil count after administering adrenaline to hypophysectomized mice. This recalls the sometimes overlooked experiment of Vogt,[7] who demonstrated a direct response to adrenaline by the adrenal cortex of the dog. This indicates the need for some reserve before Thorn's view can be fully accepted that the eosinophil response to adrenaline may be regarded as a test for the integrity of both the anterior pituitary and the adrenal cortex, whereas the response to the injection of A.C.T.H. tests the latter only. However, applying this principle, Roche and his colleagues have shown that after major surgery there may be diminution of pituitary activity. In their hands these tests have proved valuable in detecting individuals who may be poor operative risks through failure of the pituitary-adrenal system to respond in a physiological manner, and in assessing those patients who might benefit from hormone-replacement therapy.

In last week's *Journal* (p. 1165) Professor H. N. Green discussed changes in carbohydrate metabolism in shock and the relation of these changes to the pituitary–adrenocortical sytem. He has observed that the tissue response to injections of A.C.T.H.—assessed in terms of inhibition of mitosis in the skin of mice—is similar to that seen after injections of the shock-inducing agent, adenosine triphosphate. Basing his argument on this method of inhibiting tissue proliferation, Professor Green put forward the suggestion that rheumatoid arthritis represents a state of hypersensitive allergic response to some external stimulus. Nevertheless, although useful information has been gathered about the effects of the adrenocortical secretions on tissue responses, much has yet to be learnt about their influence on antibody production and on the antibody–antigen reaction.

[1] *J. clin. Path.*, 1950, **3**, 87.
[2] *New Engl. J. Med.*, 1950, **242**, 307.
[3] Sprague, R. G., *et al.*, *Arch. intern. Med.*, 1950, **85**, 199.
[4] *Bull. Johns Hopk. Hosp.*, 1950, **86**, 102.
[5] Recant, L., *et al.*, *J. clin. Endocrinol.*, 1950, **10**, 187.
[6] *Endocrinology*, 1949, **45** 403.
[7] *J. Physiol.*, 1944, **103**, 317.

## KHELLIN IN ANGINA

Khellin is a crystalline substance isolated from the seeds of *Ammi visnaga* which has a dilator action on the coronary vessels. Its action is less strong than that of amyl nitrite, but it is four times as strong as theophylline-ethylene diamine and more prolonged in its effect; in repeated doses it is cumulative. Anrep, Kenawy, and Barsoum[1] have recently described its effect in 250 patients with angina of effort to whom it was given by mouth as a liquid containing about 100 mg. of khellin. They observed definite improvement in more than half the patients studied (56%), while in 36% some degree of improvement was noted.

The claims on behalf of khellin have been investigated in this country by Dewar and Grimson[2] in selected patients with effort angina whose exercise tolerance was limited by pain. All those in whom repeated exercise led to disappearance of pain were excluded. The patients were asked to walk up and down a flight of stairs until pain occurred. Electrocardiograms were taken before and after exercise. The effect of khellin in a dose of 150 mg. was then compared with the effect of glyceryl trinitrate in a dose of 0.8 mg., observations being made on the pain and on the changes in the E.C.G. Glyceryl trinitrate removed the pain in 10 out of the 12 patients, while khellin removed the pain in 7 out of the 12 patients. The effects of both drugs were less on the E.C.G. than on the pain. In one patient glyceryl trinitrate and also theophylline caused pain before any exercise was taken, probably because of the rise in heart rate; khellin had no such action. The authors conclude from their observations that khellin is certainly effective, but that in the dose of 150 mg. it is less so than 0.8 mg. of glyceryl trinitrate. Khellin has, however, a more prolonged action than glyceryl trinitrate.

[1] *Amer. Heart J.*, 1949, **37**, 531.
[2] *Brit. Heart J.*, 1950, **12**, 54.

# REFRESHER COURSE FOR GENERAL PRACTITIONERS

# CONGENITAL HEART DISEASE—II

BY

**MAURICE CAMPBELL, O.B.E., M.D., F.R.C.P**

*Physician-in-charge, Cardiac Department, Guy's Hospital, and Physician, National Heart Hospital*

## Cyanotic Heart Disease

Diagnosis has recently become of great practical importance in the cyanotic group because of the enormous help that can be given to many of these children by a subclavian–pulmonary anastomosis or other surgical treatment. Without this the outlook is poor for most of these patients; this is strongly supported by the age incidence of the first 340 cases seen in 1947–8, as it shows a steeply diminishing curve.

| Age | No. | Age | No. | Age | No. |
|---|---|---|---|---|---|
| 0– 2 years .. | 60 | 15–17 years .. | 14 | 27–29 years .. | 6 |
| 3– 5 „ .. | 68 | 18–20 „ .. | 15 | 30–32 „ .. | 4 |
| 6– 8 „ .. | 68 | 21–23 „ .. | 10 | 33–35 „ .. | 4 |
| 9–11 „ .. | 48 | 24–26 „ .. | 8 | Over 35 years .. | 7 |
| 12–14 „ .. | 29 | | | | |

Only one in two reach the age of 7; one in five reach the age of 14; and less than one in ten reach the age of 21. The risk of death during the first four years is greater than would appear from these figures, as fewer infants have been seen. A heavy mortality rate continues up to the age of 18 or 21, and the small number surviving beyond this are relatively mild cases with a fair expectation of life. Even slight cyanosis recognizable in infancy generally means severe cyanosis later, with a relatively bad prognosis.

Apart from the general frailty of these children making them apt to die from relatively slight upsets, they have a special risk of cerebral infection because organisms that have entered the blood stream are able to pass to the brain instead of being dealt with by the lungs. Any indication that such a child is losing ground and becoming able to walk shorter distances than before is a sign of serious significance, and if anything is to be done it must be done quickly, as such deterioration is generally progressive until the child dies.

This, unfortunately, applies only to children over the age of 3. However bad the outlook in young children, and this is often because of frequent attacks of increased cyanosis, sometimes with unconsciousness, the risk of operation is greater, and the chance of improvement does not justify surgical intervention. The result is likely to be better if operation can be deferred till after the child is 5 years of age. Exact diagnosis is often impossible in infancy without special investigations which are not justifiable till later.

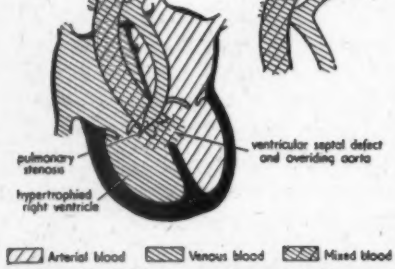



FIG. 4.—Fallot's tetralogy and diagram of Blalock–Taussig operation (end-to-side subclavian–pulmonary anastomosis).

*Fallot's Tetralogy* (*Fig. 4*).—Fortunately, the combination of pulmonary stenosis (generally infundibular) with an overriding aorta, a high ventricular septal defect, and a right ventricular hypertrophy—known as Fallot's tetralogy, though it should be called after Peacock, who described it clearly in 1858—is the most common group of congenital malformations and is present in two-thirds of these patients. This most probable diagnosis is supported if cyanosis has been present from birth or from the first 18 months of life; if there is a systolic murmur, often with a thrill, in the pulmonary area and a diminished or normal pulmonary second sound; if there is no diastolic murmur; if the heart is not enlarged; if there is no prominence of the pulmonary arc or pulmonary arteries (though less than half of them show a real sabot-shaped heart, the remainder having a relatively straight left border or even slight prominence of the pulmonary arc due to dilatation of the infundibulum beyond the stenosis); and, most important of all, if the density of the lungs on radioscopy is lighter than usual. These criteria should enable the diagnosis of Fallot's tetralogy to be made in most cases, and it is here that the operation of subclavian–pulmonary anastomosis is most likely to help. It is curious that the habit of squatting should be so common in Fallot's tetralogy; it occurs in at least four-fifths of these cases, but is seen in other forms of cyanotic heart disease, even in Eisenmenger's complex in which there is no pulmonary stenosis.

*Pulmonary Atresia.*—Cases are generally included as Fallot's tetralogy whether there is pulmonary stenosis or pulmonary atresia. The last group must now be differentiated, because the small and thin-walled pulmonary artery that is present beyond the atresia makes subclavian–pulmonary anastomosis more difficult, but not always impossible. This diagnosis must be considered when in a case otherwise resembling Fallot's tetralogy there is no systolic murmur and a rather loud second sound in the pulmonary area.

*Tricuspid Atresia* (*Fig. 5*).—When a case resembles Fallot's tetralogy in general, but the electrocardiogram shows left ventricular preponderance and also a rather larger heart with hypertrophy of the left ventricle, the diagnosis is generally tricuspid atresia with a small or non-functioning right ventricle and a defect in the auricular septum. These cases can be helped by subclavian–pulmonary anastomosis because the anomalies cause a reduction in the pulmonary blood flow, but the degree of improvement to be expected is less than in ordinary Fallot's tetralogy.

*Pulmonary Valvular Stenosis.*—In the oligaemic group Fallot's tetralogy is the most common condition, but pure

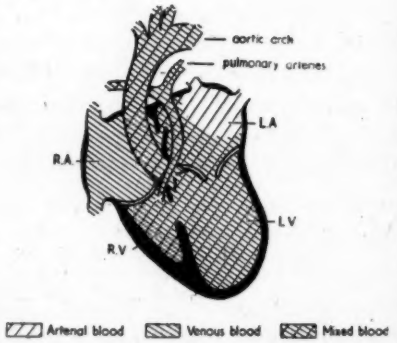



FIG. 5.—Tricuspid atresia with small undeveloped right ventricle.

pulmonary valvular stenosis with a right-to-left shunt through a patent foramen ovale is not uncommon, and this diagnosis may be suspected if there is great enlargement of the right ventricle, and if cyanosis develops later, sometimes not till early adult life. When this happens the downward course is generally rapid and the possibility of operation should be considered at once, direct surgical relief of the stenosis being indicated. In these cases the electrocardiogram will show right ventricular preponderance, often with deep inversion of T in Leads II and III. The physical signs are the same as in the acyanotic cases, but in the more severe cases the murmur may be less and the thrill may be trivial.

*Pleonaemic Cases.*—The division of those in whom the blood flow to the lungs is diminished (oligaemic) and those in whom it is increased (pleonaemic) is best made by radioscopy, but physical examination may often give a clue, as enlargement of the heart or the presence of a diastolic murmur, generally in the pulmonary area sometimes towards the apex, is much more common in this group. Even more important is the pulmonary second sound: if this is much increased and booming, or clearly duplicated, or if it is palpable, it is almost certain that large pulmonary arteries will be seen on radioscopy, and that the patient already has an adequate blood supply to the lungs, so that he cannot be helped by subclavian–pulmonary anastomosis. In the pleonaemic group accurate diagnosis is at present of less practical importance. Transposition of the aorta and pulmonary artery with septal defects, and Eisenmenger's complex, are probably the commonest lesions, the latter being the more likely diagnosis in adult patients.

### Surgical Treatment in Cyanotic Heart Disease

The outlook for these children has been completely changed by the introduction of subclavian–pulmonary anastomosis (Blalock–Taussig operation) and by Brock's more direct relief of the stenosis. The increased blood flow to the lungs allows more blood to be oxygenated and so the disability and cyanosis are both greatly relieved. When the disability is enough to justify it, operation should be advised between the ages of 5 and 10 years.

In infants the small size of the vessels produces a surgical problem of the greatest difficulty and the operation is much more dangerous and sometimes less lasting in its good effect, because the anastomosis is too small as the child grows larger. For this reason the operation should never be performed under 3, except as a life-saving emergency, and generally not till 5 years of age. From 5 to 10 is perhaps the ideal age, but there seem to be no special difficulties in older children, though the difficulties and risks are greater in those over 20.

The operation is a serious one, with a mortality of about 15%, but two-thirds of all the children are enormously improved, so that they may walk a mile or more instead of 100 yards or so, and get about all day almost normally. The polycythaemia disappears quickly and the clubbing of the fingers more slowly. The arm to which the subclavian has been divided gives no trouble.

It is important for the parents to realize that the heart condition has not been cured, and that though the outlook is much improved it is still uncertain for how long this will last. Naturally, with the increased work given to the heart, there is some increase in size; but this does not seem to be progressive, and follow-up studies so far are very encouraging and suggest that the improvement may be lasting.

In the first 100 cases operated on by Mr. R. C. Brock at Guy's Hospital 15 died, 7 could not have an anastomosis done (2 at least because of a mistake in diagnosis), and 14 were only slightly or moderately improved; the remaining 64 were enormously improved almost at once, and their condition has continued satisfactory in all except two—one with tricuspid atresia and one with a single ventricle. Many hundreds of children have now been operated on at various centres and the procedure may be regarded as an established one. The relative position to be taken by Brock's operations for valvulotomy and resection of the infundibulum still remains to be established. It may well prove to be the operation of choice in those cases in which stenosis is the main feature, which is suggested when the disability is much worse than the cyanosis. At present the relative risk seems greater, but there is no doubt that the improvement may be just as striking and dramatic, and possibly in the successful cases the good result may last for even longer.

*Illustrated by Miss Sylvia Treadgold.*

## GENERAL PRACTICE: A NEW PERSPECTIVE

### THE REPORT OF A COMMITTEE OF THE ASSOCIATION

Two years ago the British Medical Association published a report entitled *The Training of a Doctor*, with proposals for the improvement of the undergraduate curriculum. It was received with such appreciation that the Council forthwith appointed another Committee under the same chairman, Sir Henry Cohen, to carry the subject further by considering the postgraduate education of the general practitioner. The new Committee looked at this subject from a wider viewpoint than the term "postgraduate education" ordinarily suggests, and reached a proposal that there should be a post-registration period of training for general practice—a new conception in this country and one scarcely formulated in any other. It considered also the continuing education of the established general practitioner, not only by means of refresher courses and lectures, but by clinical conferences, hospital work, and consultations with specialists, as well as self-education.

It was necessary to consider the status of the general practitioner, the scope and organization of his practice, and the personal qualities his work demands. Thus the report appears under an extended title, *General Practice and the Training of the General Practitioner.*[1] It presents general practice in a new perspective, freed from certain ideas which in recent times have obscured its role and diminished its importance.

The Committee, which has put in 18 months' intensive work, consisted of 33 members, eight of whom were chosen because they were general practitioners in representative fields of practice—rural, small town, and large town. A similar number of members were associated with university teaching, and others represented the consulting branches of the profession, hospital work, and the administrative side of medicine. The six principal officers of the Association, two of whom are general practitioners, were also on the Committee.

### Apothecaries and Family Doctors

At the outset of its work the Committee was faced with the objection that conditions of practice now are such that many practitioners cannot take advantage of whatever postgraduate facilities are offered. Their immersion in routine details of practice allows them no time for study, or, if they have time, the energy and mental detachment are lacking.

The answer which the Committee makes is that its recommendations will really ease the lot of the general practitioner

[1] *General Practice and the Training of the General Practitioner. The Report of a Committee of the Association.* London: British Medical Association, B.M.A. House, Tavistock Square, W.C.1. 1950. Price 7s. 6d.

by raising his status, by stimulating his interest in the art and science of his calling, and by providing him with the means of maintaining and refreshing his knowledge and skill so that he may pursue his practice with the pleasure and satisfaction that results in efficiency.

General practice is variously regarded, sometimes as comprising only the minor responsibilities that remain after the specialists have withdrawn, sometimes as only an index to the appropriate specialists, sometimes as only a preliminary to entrance upon specialist practice. The Committee traces briefly the history of general practice. Hippocrates was a general practitioner in the sense that he took to himself the entire medical care of the individual patient; so was Galen; so were the trained leeches and monk-physicians of Anglo-Saxon and mediaeval times. It was the rise of the Royal College of Physicians and the Company of Barber-Surgeons which differentiated physicians from surgeons; and the Royal College itself, by the exclusiveness of its members, encouraged the appearance of the apothecary—originally a member of the Company of Grocers who sold drugs—as medical attendant of the less fortunate classes. The apothecary gradually rose in ability and status, though some inferiority clung to him. "What is this," cries Mr. Weston in *Emma*, "about Perry and a carriage? Is Perry going to set up his carriage, Frank? I am glad he can afford it." Another example in early nineteenth-century fiction was Mr. Hoggins in *Cranford*. "We often wished when we heard of Queen Adelaide or the Duke of Wellington being ill, that they would send for Mr. Hoggins."

The apothecary was the ancestor of the general practitioner. During the nineteenth century the supply of trained doctors for ordinary people increased, and the family doctor, now a university graduate or diplomate of a medical corporation, became an established figure in British national life. Later he became again obscured, this time by the advance of medical knowledge whereby it became impossible for one man to practise or comprehend in detail the whole field of medicine, or to possess all the necessary equipment. Even National Health Insurance, confining statutory benefit to general practitioner treatment, was an obstacle to the continuity of medical care by the general practitioner of the patient as an entire individual in his family background; and now the National Health Service Act has emphasized the administrative division.

### Routine of the Day

The Committee invited a few general practitioners to describe and tabulate their work. The accounts have some interesting touches. One practitioner, after describing his heavy day which began at 8.15 a.m., ends: "There is still time for a glance at the *Journal* or something lighter, and so to bed in the hope that a midwife won't want help with a delayed second stage." A rural practitioner gives an account of his visiting from 11.5 to 2.0—anything between 10 and 50 miles. His list of visits for one week totals 120—the largest number (25) for influenza, and the next largest (12) for acute tonsillitis. This practitioner late at night is less fortunate than his urban colleague: "11.15 p.m. Emergency call to case of coronary infarction in elderly and nervous tradesman who has been overruled at the local chamber of commerce."

The view was expressed to the Committee, by the way, that long distance deterred patients from visiting the doctor for trifling ailments, thus sparing the rural doctor one of the annoyances of his urban brother, but not all the rural members of the Committee (3) agreed with this.

The habits of practitioners are contrasted in two examples. One practitioner told the Committee that he attempted to treat most ear, nose, throat, eye, and skin cases, also psychoneuroses, and referred to the specialist only the more difficult and refractory ones; another said that except for treating conjunctivitis, blepharitis, and foreign bodies, he referred practically all eye cases to the ophthalmic specialist, and "I think I add to the skin clinics as frequently as any."

The following are the functions and responsibilities undertaken by the general practitioner, as the Committee sees them:

(1) *Continuous Care of Patients.*—The general practitioner is the patient's own doctor or family doctor.

(2) *Health Education and Preventive Medicine.*—No one else is in so advantageous a position to give advice. He knows the circumstances and job of his patient, his family problems and responsibilities.

(3) *Treatment of the Patient as an Individual.*—He must have regard to the totality of his patient, his distinctive personality, home environment, occupation, emotional make-up, medical history.

(4) *Diagnosis.*—The trivial illness, the serious, the fanciful, the real follow one another in quick succession, and it is the responsibility of the practitioner to sort them out and to decide quickly and firmly the course to take.

(5) *Treatment.*—Includes prescribing and dispensing, various technical procedures, minor surgery, psychological help, and preventive measures.

(6) *Emergency Treatment.*—Skill in first aid.

(7) *Information to Specialists.*—The general practitioner is looked to for the fullest possible information about the patient who is sent for opinion or treatment.

(8) *Aftercare and Rehabilitation.*—The patient generally needs not only convalescence and aftercare but careful supervision even after return to work.

(9) *Administrative and Legal Requirements.*—Statutory certifications, liability to give evidence in court, compliance with administrative regulations under the N.H.S.

(10) *Miscellaneous Work.*—Part-time appointments in the public health service or industrial concerns, schools, or medical institutions.

(11) *Non-medical Duties.*—Involving personal qualities which defy analysis. Answering such questions as "Should Sally marry a boy who is earning only £5 a week?" or "Should I make it up with my sister?"

### General Practice a Coherence of Specialties

The Committee discusses the relationship with specialists. It is in the return of its results to general practice that the fragmentation of medicine into specialties finds its fullest justification. The practitioner must know in what kind of illness a specialty can help him, and its scope, potentialities, and limitations. But general practice is itself a special branch of practice, with functions which in their entirety bring to the individual patient the benefit of the resources of all the other specialties. The traditional distinction in status and prestige between general practice on the one hand and any specialty on the other is wrong.

"The adequate pursuit of many specialties requires no higher ability, industry, zeal, and personality than general practice; indeed, some require less."

Both the Spens Committees were anxious that the field of practice with which each was concerned should not lose to the other on account of disparate remuneration. Sir Henry Cohen's Committee holds it undesirable that financial considerations alone should dictate the choice of a branch of practice. Every practitioner should be free to follow the branch which most appeals to him and for which he is by ability and temperament most suited, and every branch should offer reasonable prospects of material reward for efficient and successful practice.

The necessity for full co-operation between all branches and the recognition of the interdependence of special branches and general practice is insisted on. Sometimes a discovery may have revolutionary effects on methods of general practice—e.g., sulphonamides and antibiotics. Other advances may extend the scope of general practice—e.g., the specialist study of old age. The idea that general practice is an inferior branch should not be entertained by specialists, and equally it should not be accepted by general practitioners themselves. Again, the general practitioner must not be indifferent to the aid offered by specialists. It is stated that while general practitioners are usually quick to call in a surgeon when necessary, they sometimes hesitate to refer cases to a consultant physician because they regard it as derogatory to their reputation. Sometimes, if they take an interest in a special branch, they attempt procedures beyond their competence. The remedy is simply mutual understanding.

"The development of a special interest by a general practitioner is not to be discouraged; indeed, in a group practice it is desirable, and in rural practice additional knowledge is always useful. It should, however, be understood that the interest should be within the scope of general practice."

### Demands and Rewards

After reciting the personal qualities desired in a general practitioner, the Committee admits that the sum of them could be possessed only by a superman—tact, wisdom, patience, discretion, imperturbability (Osler's word), gentleness, firmness, ability to inspire confidence and trust, kindness and humanity, being all things to all men, guide, philosopher, and friend to patients of all classes, equally at ease with duke and dustman, and, along with all this, a sound medical knowledge, the ability to do patient, practical work and to apply scientific methods, observation, discrimination, selection, diagnosis, and decision. Further:

"General practice demands from the practitioner long hours and hard work, and the sacrifice of much of his home life. He will need good health and physique to stay the course. It may be added in parenthesis that the woman he marries must be prepared to share the burden and the sacrifice."

Yet the life has its compensations—freedom to order one's days, a good and dignified standing in the community, and, above all, the knowledge that by one's efforts the sick are restored to health and strength. The Committee asked several practitioners why they liked general practice. Their replies fall under three headings:

(1) *Variety of Work.*—There is pleasure in meeting the "alarums and excursions," the stimulating challenge of difficult or unexpected situations.

(2) *Doctor-patient Relationship.*—"I go into no house unbidden. Others more skilled and more learned may come, but not in the first instance. This immediately establishes a peculiar relation between the patient and his 'own doctor.' . . . This relationship I find satisfactory."

(3) *Freedom and Independence.*—"Largely his own master. Free to organize and run his practice as he thinks best."

Finally, the general practitioner should be a man of culture. The need for cultivating some outside interests is mentioned. Cultural interests will be a corrective to the tendency to complete absorption in medical life. He should play as full a part as possible in the social life of the neighbourhood—it is good for himself and his profession. One rural practitioner said, "I am in the position of the squire of former days. There is no one else in the place who knows so much about everyone, not even the vicar."

### Organization of a Practice

In a brief chapter the report sets out some information about the organization of a practice. One general practitioner in a small country town (population 3,000) told the Committee:

"The great fascination of medical work in the country is that the doctor is not a mere signpost to the neighbouring out-patient department. He has got to handle everything in the first instance himself, and still has to undertake much that could be more conveniently done in hospital but for the difficulties of distance."

A necessary condition of attendance at postgraduate courses is the provision of a locumtenent. The suggestion that there might be a central pool of permanent locumtenents does not commend itself. "Practitioners who are content with such a nomadic life without the desire to have patients for whom they are permanently responsible are unlikely to be of the best quality or to take sufficient interest in the patients of their principal." The best source is considered to be young practitioners temporarily available, such as those returning from abroad or from the Forces before settling down to permanent work, also those awaiting appointment in other spheres. The Committtee recommends that all practitioners willing to undertake work as locumtenents should notify the fact to the Medical Practices Advisory Bureau (at B.M.A. House), which would also receive applications from principals needing such assistance.

The Committee deprecates the tendency, natural enough at present, to think of the future of general practice in terms of the National Health Service. After all, that service is concerned with the environment of practice rather than with its scientific content. The changes in general practice now discernible are due rather to the natural evolution of medical science than to the imposition of official administration. To-day the accurate diagnosis of illness is increasingly important. Fifty years ago, when the resources of medicine were so much more limited, a failure in early diagnosis was of less significance, but the therapeutic arsenal is now replete with weapons of immense power for healing, and most effective when used early. This demands early diagnosis of disease, and the responsibility for that frequently rests with the general practitioner.

It is considered to be too sweeping a generalization that the general practitioner nowadays refers more and more of his cases to the specialist or the hospital. Certain advances such as the chemotherapy of pneumonia have placed in the hands of the keen general practitioner the means of treating at home many patients who would previously have been sent for hospital treatment. Three principles are laid down as requiring the attention of all concerned with the organization of medical services as well as the profession itself:

(1) The general practitioner must have time to do his work properly. One general practitioner wrote to the Committee:

"If I were asked by what methods my capacity as a general practitioner could be improved, formal postgraduate education would be quite low on my list. . . . I would say I could greatly increase my value as a doctor in general practice if I had more time and was not forced by financial considerations to take on so much work. With time one could help the functional and psychological cases so much more. . . ."

(2) The medical practitioner must not be isolated either from other medical services or from his colleagues. He should have diagnostic and ancillary services within easy reach.

(3) He must have leisure—free time for professional reading, for attendance at postgraduate courses and other professional meetings, for investigation and research in his own practice, either for his own interest and satisfaction or as a contribution to wider studies. The family doctor must be a cultured member of the community.

## FIRST THREE YEARS IN GENERAL PRACTICE

### Post-registration Training

Having surveyed the ground, the Committee next turns to the training of the young doctor who has selected general practice as a career. It believes that much energy in his first few years of practice could be saved and efficiency promoted if the new recruit to general practice received some systematic training for his life's work. Accordingly the main recommendation of the Committee is:

That a period of three years should elapse between registration and the assumption of independent general practice, and that this period should be spent in preparation directly designed for general practice, just as entrants to other special branches of practice expect to devote several years to training for it.

For the first of the three years the young practitioner would act as trainee assistant to an established general practitioner; the second year would be spent in appropriate resident hospital appointments, and the third year would provide supplementary training at the choice of the trainee.

The organization of the training would be in the hands of a postgraduate committee and a full-time or almost full-time dean appointed by each university or medical school, the committee to include representatives also of the regional hospital board, hospital governors and medical staffs, local medical societies, Divisions of the B.M.A., and local medical committees.

During this period of training the practitioner should receive adequate remuneration and should be allowed and expected to accept a degree of personal responsibility appropriate to his experience. The principle of providing a "living wage" while learning the job was advocated in the Spens (Specialist) Report, and should be applied to the general practitioner undergoing training. It is conceded that the qualities of a good doctor cannot be taught, but early direction can be given to the use of those qualities in practice, and so the young practitioner may be saved from many mistakes and pitfalls. The transition from the sheltered atmosphere of the hospital to the stark responsibilities of practice often imposes a severe emotional and physical strain. "I have not forgotten," wrote one practitioner, "the shock I received when I first went into general practice after two years as a resident."

The following is the scheme recommended by the Committee:

First year: Training under the supervision of a general practitioner.

Second year: Training in specially designed, preferably resident, hospital appointments; it is likely that these will be taken predominantly in hospitals under the administration of regional hospital boards.

Third year: A choice of opportunities, including: (i) senior training appointments in hospital departments for varying periods of one to three months; (ii) simultaneous clinical assistantships in different subjects; (iii) further assistantships in general practice; (iv) locum appointments in approved general practices for a total period not exceeding three months.

A year is considered desirable as the period of trainee assistantship because in general practice a year forms a cycle of work, with its seasonal changes. For resident hospital appointments also a year seems not too long. The training would be given largely outside teaching hospitals but would be organized and supervised by the academic body mentioned in the first recommendation. It is added that the trainee should not be used as an ordinary assistant in general practice or as a means of lightening the burden of hospital staffs. His programme of work should be carefully planned to give properly balanced instruction, with reasonable time for leisure and relaxation.

### Period of Compulsory Service

Spatchcocked into any such scheme is the requirement of 18 months' compulsory service with H.M. Forces. The Committee has inquired whether any portion of that period could suitably count towards the three-year training period it has laid down, and, after consultation with the heads of the three medical services of the armed Forces, it recommends that the compulsory 18 months' period should count as 12 months of the training for general practice.

The statements of the three Directors-General are published in the report. They were asked whether it was right to say that so far as training and experience for a medical career were concerned the period of compulsory service was lost to the young doctor. To this they all replied "No." They were further asked whether facilities were available for work in civilian hospitals. The Navy said that every encouragement was given to young medical officers to attend both naval and civilian hospitals; the Army that, generally speaking, there were no facilities for work in civilian hospitals; the Royal Air Force that, while there was no set arrangement, medical officers were encouraged to visit Service and civilian hospitals where this was practicable. To a further question on whether any adjustment in training or duties could be made to give them a greater professional value for subsequent civilian practice, the Navy and the Royal Air Force considered that owing to the short period the National Service man served it would be impossible to give him more professional training; the Army, that it depended on the syllabus, but that, if training in preventive medicine and in positive health was a necessary factor, the young doctor would have such experience during his Army training.

The Committee adds that the allowance that the 18 months' period of national service should count as 12 months towards the three-year training should not affect the requirement that one year should be spent under the supervision of a general practitioner. It believes that if the medical officer knew that his period of compulsory service was going to contribute towards the preparatory period for general practice he would be less likely to feel that he was wasting his time and more ready to take advantage of any facilities for civilian practice that were open to him.

### The Trainee Assistant

The teacher who takes a "trainee assistant"—a better name than "apprentice"—must be a general practitioner of not less than five years' standing. Such a practitioner accepts a new responsibility, and he may have to exercise some forbearance; on the other hand, he may discover a new zest for the practice of medicine in the training of an enthusiastic entrant. Each principal must develop his own methods: precept, example, and discussion should all play a part.

The young general practitioner also has a great deal to learn on the practical administrative side of medicine. Probably he leaves hospital knowing nothing of such matters as how to obtain a district nurse, what to do about a patient with tuberculosis, the regulations of the N.H.S., the relations between himself and the medical officer of health, and the proper use which is available to him of the facilities at the local hospital. These and many other matters may be imparted in the form of lectures, which would be best given in the intern year. The Committee commends a synopsis of five such lectures given by a general practitioner to students in a London teaching hospital.

The hospital appointment in the second year should preferably be, not in a teaching hospital, but in one of the larger hospitals under the regional hospital boards, which are rich and largely neglected mines of clinical material. The teachers would be members of the medical staff. The purpose of the teaching would be, not to increase the trainee's acquaintance with rarer diseases, but to gather such knowledge and experience as would enable the young practitioner to undertake independent treatment of the kind of case that presently will fall within his scope and to recognize where specialist help must be sought.

In the third year he has a wide option. Appointments specially designed for research are not necessary or desirable for the majority of trainees, although, of course, aptitude for research should be cultivated. Some further instruction in psychiatry might be given during this period.

### Continuing Education

The Committee finally addresses itself to the continuing education of the general practitioner throughout his active life for the purpose of preserving and increasing his technical competence and affording him contact with hospital practice and with advances in the diagnosis and treatment of disease. Criticism of many of the present postgraduate courses was freely expressed in the Committee. Some of them were said to be insufficient in extent and inadequate in content. Many of the teachers tended to concentrate on the description of rare diseases outside the range of general practice.

Advice is given on the arrangements for refresher courses such as a practitioner will take perhaps once every few years. The postgraduate committee already referred to and the dean appointed by the university will collaborate for this purpose with hospitals, specialists, and medical committees and societies in the area. The courses should be accompanied by educational work in hospital, clinical conferences, and ward rounds. The most useful arrangement is a two weeks' course; a one-week course is over-intensive. Week-end courses may be useful for special subjects. The kind of instruction needed is summarized as: (1) refreshment of basic knowledge; (2) instruction in recent advances; (3) presentation of new knowledge related to the practitioner's own approach to his practice—that is, to the view of the patient as a whole; and (4) periodical restatement of the contributions of other sciences to medicine.

The tutorial method is preferred wherever possible. Classes should be limited in numbers. Set lectures should be at a minimum: discussions and demonstrations with ample time for questions are better. Lectures and discussions should be grouped around a single theme, as, for example, hypertension, arthritis, endocrine therapy. The report contains a number of illustrative notes on the needs of general practitioners in certain subjects such as psychiatry, ophthalmology, dermatology, and occupational health, submitted by practitioners with special experience in these branches.

"Everything possible should be done to make the postgraduate course a memorable event in the life of the practitioner. He should return to his practice with not only a 'brain dusting' but new knowledge and mental recreation, and the benefit will be passed on to his patients."

The report also gives suggestions for the arrangement of more regular local courses and conferences. Here again the postgraduate dean comes into the picture, but also the local medical

societies and B.M.A. Divisions. The most convenient time of year, day of week, and hour of day for such events is discussed, also the use of films, the value of "Brains Trusts," the arrangement of meetings with representatives of other professions, such as teachers, lawyers, social workers, and journalists, and the organization of courses at the local hospital.

### General Practitioner and Hospital

The divorce of the general practitioner from the hospital is deplored by the Committee. There are cases, however, in which such contacts are close and fruitful. One practitioner who gave evidence presented the following summary of the work he carried out at the hospital:

(1) Midwifery.
(2) Routine care of cases admitted either as medical emergencies or for operation by one of the visiting consultants.
(3) Assisting at operations on these cases.
(4) Consultations with visiting specialist staff.
(5) Minor surgery and accident emergencies, for which a weekly rota of the local doctors is provided.

Inquiry has shown that many practitioners would like to attend as postgraduate students in the out-patient departments and on ward rounds, and some of them would be prepared to apply for clinical assistantships, especially in such branches as paediatrics and dermatology. The Committee recommends the creation of such posts in all suitable hospitals, not with a view to diluting the hospital staff nor primarily for the sharing of the burden of routine work, but for the education of the visiting practitioner. It is thought that such posts could exercise a helpful influence on conditions of practice under the N.H.S. and counteract those tendencies which limit the scope and interest of the general practitioner. The Committee also supports from an educational standpoint the increasing demand for general-practitioner hospitals and wards, and it urges that when his patient is in hospital the general practitioner should be permitted at all reasonable times to visit him and that the hospital staff should keep the practitioner in touch with the patient's progress.

There remains the question of the general practitioner's reading. Casual reading is of little value to the members of a learned profession. It is suggested that the periodical is of greater value to the practitioner than the book or monograph, the book being to some extent out of date as soon as it is published. What is in the periodical to-day may not be incorporated in the book for a couple of years. The complaint is sometimes made that even the general medical journals do not cater adequately for the general practitioner. "The complaint is usually unjustified and indicates a desire for 'spoon-feeding' and a lack of appreciation of the basis of general practice." Reference is made to the features of special interest for general practitioners in the *British Medical Journal*. But the general practitioner will add greatly to his efficiency by also reading articles which appear specialist in character, and it is suggested that he should read each week at least one article which might be designated "high-brow," and endeavour to understand its message and significance. He should also read the scientific leading articles in the weekly periodicals which from time to time portray the changes in the countenance of medicine. The medical library is an essential instrument in the education of the practitioner. Nor should he forget in his reading some of the more important books on contemporary affairs and progress in other fields than medicine; and above all he should fortify himself by returning to the imaginative and creative works of permanent value.

In closing this opportune, most readable report—"report" is a word of hardly sufficient dignity to describe it—the Committee acknowledges that the fulfilment of its recommendations will require a larger number of doctors and that each doctor should have a smaller number of patients in his care. Readjustments of methods of remuneration will therefore be necessary. But the desired increase in the number of recruits to the profession as a whole and to general practice in particular may be partly dependent upon the raising of the standards and status of general practice. To that end the work of Sir Henry Cohen's Committee will have made an outstanding contribution.

## THIRD WORLD HEALTH ASSEMBLY

### FUTURE PLANS

Speaking at the opening on May 8 of the Third World Health Assembly Mr. TRYGVE LIE, Secretary-General of the United Nations, said that in less than two years of full operation as a permanent specialized agency of the United Nations the World Health Organization had made a fine start. The limitations on the programme W.H.O. wished to adopt for 1951 and the related budgetary restrictions arose primarily from the political, economic, and psychological consequences of the "cold war." They certainly did not arise from any lack of human needs. The doctors, scientists, and others who served the specialized agencies of U.N. were a strong influence for peace. All their work was directed at creating economic, social, and humanitarian conditions that would encourage a more peaceful behaviour by men and States.

The supreme challenge of the second half of the twentieth century, and especially of the next 20 years, was not expressed in the ideological and power conflict that monopolized the headlines to-day: the challenge was presented by that great majority of the population of the world whose poverty, hunger, and insecurity must be substantially remedied if there were not to be new and disastrous upheavals.

Dr. KARL EVANG (Norway), who followed, pointed out that a number of countries had announced that they no longer considered themselves members of W.H.O. "What makes this unjustifiable and inexplicable withdrawal the more hurtful to the interest of international health is that the countries in question constitute a group of nations which we, for several reasons, need badly in W.H.O. We would like again to stress that the doors are open for them to rejoin us." He then described the budget of $7.6m. voted by the Second World Health Assembly as completely inadequate to meet the health needs of the world. It threatened to reduce W.H.O. to an administrative, planning, and collecting organization only, leaving very little money for practical work in the field. Another setback suffered by W.H.O. was that the programme of technical assistance for economic development in underdeveloped countries had not yet materialized. On the other hand, one could survey with satisfaction the development of W.H.O. activities in a growing number of countries. Governments were rapidly realizing that many health problems required international action and advice for their solution. Governments were more and more willing not only to accept but also to offer advice. If there were millions of people still living in ill-health and misery to-day it was not so much for lack of knowledge but for lack of application of knowledge.

Dr. BROCK CHISHOLM, Director-General of W.H.O., then spoke on the need for co-operation by member governments (May 20, p. 1215). Some governments failed to appreciate fully the significance of health in the promotion of human prosperity.

### Election of President

At the second plenary session RAJKUMARI AMRIT KAUR, the Health Minister of India, was unanimously elected president. Princess Amrit Kaur has had much experience as a social worker and was for 16 years secretary to Mahatma Gandhi. After expressing her gratitude to the Assembly she said that she believed they had laid the foundations for promoting their great work on sound lines. They had every reason to feel gratified that the growth of W.H.O.'s activities had been steady and many-sided, and above all particularly helpful to underdeveloped countries. The annihilation of time and distance within the past few decades had contributed to make the health of all countries an indivisible whole. Even in the days of comparative isolation there were times when pandemics of cholera, plague, and influenza overflowed their natural boundaries and spread with devastating effect over many continents. The danger was all the greater to-day, and even from the standpoint of self-preservation it had become imperative to provide international co-operation in the field of health to the greatest possible extent. It was gratifying to note a growing recognition of the homogeneity of the human race in relation to its needs

and aspirations and that the wealthier and better-organized nations were promoting an active effort to improve the health and standards of life of their less-favoured brother nations. Those assembled there, as well as the people they represented, were grateful to the U.S.A. for the large measure of help that had been forthcoming from them, though permanent relief must eventually come from the organization of joint effort by all nations, big and small.

### Future Policy

On May 9 and 10 delegates debated W.H.O. policy. The first speaker, Dr. M. DE LAET (Belgium), pleaded for better co-ordination between the central technical services of W.H.O. and its advisory services to governments. The regional offices, which were engaged in actual field work, should enjoy a larger degree of autonomy and greater financial resources, while headquarters at Geneva, which was mainly concerned with the collection and dissemination of information, should emphasize decentralization.

Dr. S. HAYEK (Lebanon) called for assistance in health education of the Lebanese population and for other essential programmes, among them malaria control and environmental sanitation. Praise for the "incontestable progress" achieved by W.H.O. in the past year came from Professeur JACQUES PARISOT (France), who declared that the advisory services rendered by W.H.O. were of paramount importance. No country should be interested only in the material advantages it could obtain from W.H.O. Referring to the budgetary limitations imposed on W.H.O., he suggested that, instead of launching too many programmes, the Organization should limit itself to a few activities which could be successfully and efficiently undertaken.

Speaking for Thailand, Dr. SVASTI DAENGSVANG expressed his country's appreciation for the malaria control demonstration undertaken there by W.H.O. and Unicef, and for other assistance rendered. Dr. PAVLE GREGORIC (Yugoslavia) praised the principle of equality among all peoples applied by the Organization. Yugoslavia was a firm believer in international action and welcomed the co-operation of all countries in W.H.O.

Dr. MELVILLE MACKENZIE (United Kingdom) declared himself satisfied with the work of the Organization during the past year, and praised the high standards of the reports of W.H.O. expert committees, which "have produced for governments the most modern ideas both in research and in practical administration under each subject." He suggested that the Organization's efforts be restricted to a few important public health problems, which lent themselves to international procedures. His government, which was responsible, apart from the United Kingdom, for the health of 60,000,000 people in other parts of the world, attached the greatest importance to the existence and proper functioning of W.H.O. and would spare no effort to ensure its success. Dr. WALFRIDO DE LEON (Philippines) said that several workers from the Philippines had been able to study abroad, thanks to W.H.O. Fellowships. The Philippines could offer useful information to W.H.O. on many health problems, such as leprosy and malaria, which the national health administration were tackling successfully.

Dr. S. W. R. C. BANDANARAIKE (Ceylon) drew the attention of the Assembly to the fact that, for next year, the regular budget was very limited, and that provision was made for supplementary sums to be obtained from the United Nations scheme for technical assistance to underdeveloped areas. But, he added, that would be a melancholy repetition of the line of thought which induced W.H.O. last year to provide for a supplementary budget which had not materialized. Speaking for India, Dr. K. C. K. E. RAJA called for an extension of epidemiological studies, for more positive action against such communicable diseases as cholera, and for closer integration of these activities within W.H.O. He also considered an extension of the Fellowship programme desirable, and called for an expansion of training facilities in underdeveloped countries.

Dr. J. R. TOGBA (Liberia) urged W.H.O. to grant his country all assistance possible. He asked for help in environmental sanitation, road construction, malaria and venereal-disease control, and Fellowships at the undergraduate level. Dr. ABDUL H. TABA (Iran) said that, thanks to the help of W.H.O., Iran was now able to wage an active, nation-wide campaign against malaria. In some areas the ravages of malaria and other diseases were so serious that there were whole villages where a really healthy child under 2 years of age could hardly be found. Dr. ALFRED KHAUM (Austria) considered the setting up of a regional office for Europe to be one of the most important tasks confronting the present Assembly. A plea for expansion of health education was made by Dr. J. OREN (Israel), who urged that W.H.O., in co-operation with other specialized agencies of the U.N., undertake first an integrated programme of health education for children, to be followed by health education activities for the general public. Dr. LUIS F. THOMEN (Dominican Republic) hoped that the integration of the Pan-American Sanitary Bureau with W.H.O., which was now taking place, would be completed without delay, and the establishment of the P.A.S.B. as the W.H.O. Regional Office for the Western Hemisphere was also welcomed by Dr. HEITOR FROES (Brazil).

Mr. MARIO COTELLESSA (Italy) said that an appropriate procedure should be found to allow all member States to participate more actively in the work of W.H.O., and that the W.H.O. programme should be revised to conform more closely with present conditions, which in many countries had changed since the immediate post-war period.

### Four-year Plan

A four-year plan for world health has been outlined and is due to start in 1952. The Committee on Programme, discussing the plan on May 10, considered the following services to be essential.

(1) The "traditional" international services, which are of global rather than of regional importance, and include health statistics, international sanitary regulations, application of international standards for biological and pharmaceutical preparations, work on addiction-producing drugs, and scientific publications.

(2) Co-operative services, jointly with the United Nations and other specialized agencies.

(3) Education and training of medical and auxiliary personnel.

(4) Advisory and demonstration services to governments in the control of communicable diseases. In addition to the "big three"—malaria, tuberculosis, and venereal diseases—W.H.O. is to assist governments in controlling typhus, plague, cholera, bilharziasis, smallpox, leprosy, and trachoma.

Other services to governments, such as organization of health services; physical, social, and mental well-being, with specific emphasis on maternal and child health; nutrition, sanitation, and health education. The scheme includes rendering assistance to governments in obtaining medical supplies.

The next day the Committee unanimously adopted a resolution presented by Dr. MELVILLE MACKENZIE (United Kingdom) asking the Assembly to give its general approval to the four-year programme. The resolution also asked the executive board to prepare more detailed plans.

In the course of the debate on the four-year plan the delegations from India and Pakistan asked that special emphasis should be placed on undergraduate and graduate training of health personnel, on development of health and vital statistics, and on medical supplies. Dr. J. D. MACCORMACK (Ireland) called upon the advanced countries to make sacrifices now to provide assistance for the less privileged nations.

The world shortage of physicians and other health personnel was discussed during two sessions of the Committee on Programme on May 12. All delegates agreed that the shortage, even in the most advanced countries, was serious. In underdeveloped countries the ratio in some cases is as low as one physician to 100,000 of the population. In advanced countries the situation in rural areas is said to be often as bad, since for economic and other reasons doctors tend to establish themselves mainly in the larger towns and cities. To remedy the problem W.H.O. was requested to subsidize and enlarge existing medical, public health, and nursing schools. Some speakers recommended that W.H.O. create such schools where needed. Dr. M. KHALIL, Bey (Egypt), suggested that W.H.O. should not limit

its aid to medical schools only, but should also recognize and assist schools providing undergraduate training to raise their standards. According to Dr. K. C. K. E. RAJA (India), W.H.O. should set teaching standards for both undergraduate and graduate schools, as well as establish the requirements for medical degrees, such degrees to be recognized as valid the world over.

Another problem discussed was that of attracting physicians from cities to rural areas. Dr. ANDRIJA STAMPAR (Yugoslavia) thought that no compulsion should be used. Dr. NAIL KARABUDA (Turkey) declared that compulsory medical service had been tried in his country for a time, young doctors being asked to serve a few years in a rural district before being allowed to settle in a large town, but this had failed. The same system is now being tried in Greece, according to Professor GEORGES IOAKILOGLOU, a law to that effect having been passed a few months ago.

Dr. Stampar thought the best way to attract young physicians to rural areas was to provide them with adequate pay, good housing, and efficient means of transport. To these Professor A. H. H. RODHAIN (Belgium) added small, well-equipped, rural hospitals, such as those established in the Belgian Congo, where doctors can practise and feel they are not losing their skill. Dr. DUJARRIC DE LA RIVIÈRE (France) pointed out that in his country rural doctors were better off financially than the majority of those in the cities.

At the end of the session the Committee on Programme adopted a resolution recommending the Assembly to call the attention of countries to the necessity for adequate training of medical and other personnel essential for health care; and to consider that the training of doctors should be so balanced as to produce a body of men who can practise prevention as well as diagnosis, and social as well as clinical pathology, and psychosomatic medicine.

The Committee on Programme has appointed a working party to examine the possible dangers of cholera spreading to the Eastern Mediterranean region by means of Mecca pilgrimages, and it will also send teams of experts to special areas of Asia and Africa to launch anti-plague campaigns.

Indonesia, Viet Nam, Cambodia, and Laos have been admitted to membership of W.H.O., and Southern Rhodesia has been admitted as an associate member.

## REFRIGERATED BONE IN SURGICAL PROCEDURES

### ROBERT JONES LECTURE

The Robert Jones Lecture was delivered at the Royal College of Surgeons on May 3 by Professor PHILIP D. WILSON, of New York, who spoke on the use of preserved bone in surgical procedures.

During the recent war, Professor Wilson said, orthopaedic surgeons often made use of fresh bone obtained from amputations. This bone caused no apparent unfavourable reaction in the host and it served its purpose well. The commercial development of low temperature refrigeration led to the preservation of homogenous bone, and in April, 1946, a deep freezing unit was installed at his hospital, the Hospital for Special Surgery, New York. The earlier results with refrigerated transplants appeared to be satisfactory, and since then transplants of this type had been used with increasing frequency.

Professor Wilson said that his own experience with refrigerated bone transplants at his hospital, up to January 1 last, covered 307 operations on 259 patients. A series of experiments was first carried out on dogs, and the conclusion reached was that when transplants of autogenous and of refrigerated homogenous bone were placed in the leg the resorption of the former began earlier and progressed more rapidly, but that in the end the process was complete in both. Signs of repair appeared at the end of three weeks with the autogenous graft and at the end of six weeks with the refrigerated.

Histological studies of specimens of autogenous and refrigerated bone transplants recovered at secondary operations on a number of patients had been made. Three or four weeks after transplantation active new bone formation could be detected, and the healing process seemed comparable in both the fresh autogenous transplants and the refrigerated transplants. Whether the graft was autogenous or homogenous seemed to make no difference ultimately. In general, with refrigerated transplants the wound healing was the same as if autogenous bone had been used. No unusual reactions were seen, and there was no evidence of incompatibility. The incidence of wound infection in the 307 operations was only 2.6%, and in the whole series there was a loss of bone in only two cases.

Analysis of the 244 operations which it had been possible to follow up showed that the number of failures was only 27. In the group in which grafting had been undertaken on account of scoliosis there had been uniform success. In cases of bone tuberculosis the failures numbered 7 as compared with 11 successes. Tuberculosis, of course, presented a difficult problem. In cases of osteomyelitis 9 successes were recorded in 11 patients.

Professor Wilson then showed a film illustrating the whole process of preparing the excised bone for refrigeration and the subsequent insertion of the bone in another patient. The film emphasized the care with which the bone was made ready for the refrigerating chamber. The removal of bone fragments in orthopaedic operations, also the removal of shafts of bones, was shown, together with their subsequent treatment. The soft tissues were separated away, any joints in the amputated limb were disarticulated, the articular cartilages were removed, and the bone remaining was subjected to a careful and prolonged sterilization, with rigorous inspection afterwards to ensure that sterility had been achieved. Finally the sections and fragments were placed in sterile tubes and jars, which were sealed and labelled, and placed in the refrigerator, the temperature of which ranged from −10 to −20° C. The donor was always tested for venereal disease. The film also showed how the replacement bone was selected and inserted in the wound and the manner of its fixation. In the case of large transplants bone chips were added to assist union.

The great advantages of the procedure were (1) that the required bone was immediately available in an emergency; (2) that there was abundance of material; (3) that from the stock in hand in the "bone bank" the exact type of bone best suited to the case could be selected; and (4) that a second operation was avoided.

The average length of time that the bone remained in the refrigerating chamber was 54 days. The lecturer suggested tentatively that a limit should be set for the time of preservation, which should not be longer than one year. With very long preservation there was a danger of dehydration. The rationale of the procedure depended upon the understanding of what happened when implantation took place. Bone was a living tissue, and therefore dependent upon the nutrition which it received through the circulation. When it came to a consideration of homogenous bone transplantation there was no ground for claiming that any living elements survived subzero temperatures for long periods. He believed the evidence to show that the grafted bone united rapidly with the host, and that the results were comparable with those obtained with fresh autogenous grafts. The bone was inert and gave rise to no inflammatory reaction.

Altogether the experimental evidence suggested that while an autogenous graft had some advantage over a refrigerated homogenous graft in that healing and resorption took place more rapidly, in the end the results were the same. Histological studies showed no significant difference in the rate or method of repair. He emphasized that a study of the clinical results of the use of homogenous transplants in his own 307 cases showed the bone to be well tolerated. Follow-up studies showed successful results in 85% of cases. With transplants which had been preserved for more than one year the failure rate was higher. He thought the "bone bank" was a safe and practical proposition.

A view of part of the exhibition. In the foreground an exhibit on the history of the thermometer; on the right the early development of the stethoscope.

# MEDICINE IN 1850

## EXHIBITION AT THE WELLCOME HISTORICAL MEDICAL MUSEUM

Professor Henry Sigerist, lately of Johns Hopkins, will formally open on Tuesday next, May 30, an exhibition which has been arranged at the Wellcome Historical Museum, 28, Portman Square, by the Director, Dr. Ashworth Underwood. The general title of the exhibition is "Medicine in 1850," and this has been interpreted widely. The intention has been to indicate the state of medicine generally a century ago, but Dr. Underwood has wisely included exhibits illustrating some influences which had been at work some years earlier and others of which the full impact was not felt until perhaps a decade later.

One large room is devoted to the basic sciences. There is a small physics section which includes one of Volta's original "piles" and Lord Kelvin's quadrant electrometer. In another case devoted to biology are shown some of the plates which Ehrenberg first published in 1838 in his work on the infusoria. Here, too, there is a preparation of the ear and related structures in the horse which is the work of Georges Cuvier himself.

Part of this exhibit is an unfamiliar lithograph by T. H. Maguire of Charles Darwin as he was at the age of 40 in 1849. Much later, and indeed much finer, is an etching by P. A. Rajon after W. W. Ouless shown in its first state of engraving and then in the second state, this latter being signed by Charles Darwin as well as by Ouless. Pictures of William Harvey and of John Hunter lead naturally to a group of exhibits under the general headings of physiology and anatomy. Incidentally, the portrait of Harvey exhibited is a very rare etching by Richard Gaywood.

There is a set of Galvani's original instruments with which he performed some of his experiments on "animal electricity." François Magendie and Claude Bernard are represented here, and William Beaumont (1785–1853) receives honourable mention with, of course, Alexis St. Martin. An important exhibit is the fine portrait in oils, hitherto undescribed, of the founder of physiological chemistry, Justus von Liebig. The portrait, which is signed and dated, was painted by C. F. W. Trautschold in 1845. In the anatomical section there are scarce works by Sir Charles Bell (1774–1842) and Jacob Henle (1809–85). The first edition of *Gray's Anatomy* (1858) is well displayed, and there are some fine early anatomical models and preparations. Of particular interest are the original daguerreotype photomicrographs by Léon Foucault, which are set up between some early dissecting microscopes and the type of camera lucida which Lord Lister's father first applied to the microscope. Alongside these early microscopes in the section on pathology are some of the fine coloured plates of Cruveilhier (1791–1873).

Another room is devoted to the developments in the art and science of diagnosis and treatment. Prominently displayed is the stethoscope which Laënnec himself presented to Dr. Bégin, a French Army surgeon, together with the first edition of Laënnec's great book. These are surrounded by all the many varieties of monaural stethoscopes which were soon afterwards in use. There are specimens in ivory, in wood, and in vulcanite. The binaural stethoscope was invented in America, and there is shown also what was probably the first of these instruments to reach this country from the United States.

Marey's sphygmograph is displayed attached to a model of the wrist and hand, and near by are the portraits and original papers of William Stokes (1804–78) and Sir Dominic Corrigan (1802–80). Thomas Addison, of Guy's Hospital, is given pride of place in another show-case, and near him is a portrait of Robert James Graves, of Dublin. From the first descriptions of Graves's disease and Addison's disease it is but a step to a very full exhibit devoted to the work of Richard Bright (1789–1858) in which are shown some of the original coloured plates made for his book. There is, too, a section giving the first descriptions of the different palsies, and alongside this are some of the earliest ophthalmoscopes and other diagnostic instruments.

In the centre of this room there is a fine display tracing the history of the thermometer from the earliest experiments in recording temperature to Sir Clifford Allbutt's modifications of Aitken's instrument, a final stage in a long development which led to the appearance of the modern form of clinical thermometer. Behind the thermometers there is a remarkable collection of leech cages, lancets, and "automatic scarificators." In the same room there are sections devoted to pharmacology a hundred years ago. Near this exhibit James Blundell (1790–1877) presides over an exhibit illustrating the early development of blood transfusion. In the same case there are some of the earliest-known hypodermic syringes.

The Wellcome Historical Museum and its Director are to be congratulated on another excellent exhibition, which will be open to the public from Wednesday, May 31. It will be possible to see the exhibition daily between the hours of 10 and 5 except on Sundays.

---

Dr. A. L. Chapman, chief of the division of chronic disease of the U.S. Public Health Service, said that if all Americans could be medically examined some disease or physical defect would be found in nine out of ten of them. Dr. Chapman told the American Tuberculosis Association in Washington that such routine investigations should include tests for heart conditions, tuberculosis, and diabetes, which would be caught in their early stages, and also for venereal diseases, anaemia, high blood pressure, obesity, and defects of vision and hearing. He remarked that multiple medical examinations had been introduced in several United States towns, and said they did not solve the problem of the control of chronic disease but they contributed substantially to its solution. "Generally," said Dr. Chapman, "the American people are healthy . . . they are at a productive peak, but there is every reason to believe that by multiple screening methods literally millions of people can be made aware of hidden or latent chronic illnesses and physical defects much sooner than happens to-day."

# Nova et Vetera

## A NEWLY DISCOVERED PORTRAIT OF WILLIAM HARVEY

There is a universal desire to know something of the physical appearance of our great predecessors. Not a few feel that they appreciate better the work of a man when they have his image before them. This has led to many fantastic misrepresentations of the heroes of science, for of the appearance of some of the greatest of them we have, in fact, no record at all. Thus the features of Hippocrates, Aristotle, Archimedes, Galen, among the ancients, are quite unknown. We have no reliable representation of any of the mediaeval masters. Among the moderns of our own country there are no portraits of, for example, William Gilbert and Robert Hooke. Nevertheless from the sixteenth century onward the art of the woodcut and later of the copperplate induced men to attach portraits of themselves to their printed books. Thus we have adequate portraits of most of the moderns, even when paintings are lacking. Indeed, of some of the most famous—William Harvey among them—we have too many representations. In 1913 the late Sir D'Arcy Power published a volume containing prints of numerous alleged pictures and engravings of him. But the discoverer of the circulation of the blood was a very industrious man, with considerable practice, and of reticent personal habits withal. Thus it is obvious that he could not, and would not, have spent days, time after time, sitting for artists. Only a fraction of the numerous portraits of Harvey are therefore worth serious consideration as containing any reliable record of his appearance.

Mr. Geoffrey Keynes has recently submitted the portraits of Harvey, real and alleged, to a searching and critical examination. He has put together the results of his investigations in a most attractive and beautifully illustrated volume.[1] It contains the substance of his Thomas Vicary Lecture for 1948 before the Royal College of Surgeons of England and includes some twenty-odd of the more significant "portraits" of Harvey. Evidently most even of these must be at best derivatives and at worst spurious. Mr. Keynes concludes that of the portraits hitherto generally recognized as of Harvey all represent him as somewhat advanced in years, or even aged. Those to be seriously treated are only six in number.

Best known is the portrait at the Royal College of Physicians ascribed to Cornelius Janssen (1590–1664), who worked in England till 1648. It is traditionally said to have been in possession of the College before 1666 and has therefore survived two fires of London. It has been damaged, and the right hand very badly repainted. Most would probably say that it suggests a man of somewhat over 60, an age which Harvey reached in 1638. This portrait is the source of the well-known Faithorne engraving. In the collection of Dr. William Hunter at the University of Glasgow is a portrait once in the possession of Dr. Richard Mead. It has suffered considerably from overcleaning. It represents Harvey sitting, with buildings of Rome in the background, while before him is a book which can be dated at 1645, when he was 67. In the picture he seems to look older than that.

A third representation is the bust by Edward Marshall (1598–1674) in Hempstead Church, Essex, where Harvey was buried. Mr. Keynes considers that it was either made during life or from a life-mask and not, as has sometimes been thought, from a death-mask. Most, we think, would place the age as of a man in the late fifties.

Other representations which Mr. Keynes regards as of great interest are the portrait in the Kent and Canterbury Hospital and that at Ditchingham Hall, in Norfolk. This latter represents an aged and tired man of great dignity, and is perhaps the most attractive of all the Harvey portraits. It once belonged to Dr. Richard Bright (1789–1858), of "Bright's disease," but its pedigree cannot be traced beyond him further than the end of the eighteenth century. Lastly, among the more important sources, Mr. Keynes includes an unhappy etching which he ascribes to Richard Gaywood, a pupil of Hollar. It suggests an irritable, punctilious old man suffering from bodily discomforts; obvious among them is a stuffy and very ill-fitting academic dress. This picture, we feel, is perhaps best forgotten, except by iconographic experts.

All these and many others Mr. Keynes discusses with his usual distinction and critical learning. But there is yet another portrait of the very highest interest. To tell the story of this it is best largely to use the words of Mr. Keynes himself.

"In his *Life of Harvey*, 1897, Sir D'Arcy Power made a cursory reference to pictures at Rolls Park, but had apparently not thought them worthy of investigation, though he reproduced in his *Portraits of Harvey*, 1913, a picture of a gentleman in a falling ruff which had formerly been at Rolls Park and was supposed to represent William Harvey. This picture had been removed from Rolls Park."

In fact, it represents Harvey's brother Eliab, who was the most prosperous of the seven brothers, of whom William was the eldest.

Rolls Park, in Essex, is the property of a descendant of Eliab in the female line. It is unoccupied and has suffered considerable damage from bombing. Mr. Keynes shows that one of the rooms there contained a portrait of Harvey's father and of his seven sons, including Eliab and William. They had all been fixed to the walls with plaster surrounds. Two had been hacked out and stolen. Of the remainder Mr. Keynes writes:

"Examination of the portraits has now established their authenticity. They all bear the names of the subjects. The central panel shows the first Thomas Harvey in 1614 at the age of 64. The ovals represent the seven sons, beginning with William, the eldest. . . . The pictures having been fixed in the wall for nearly 200 years, have never been tampered with, though they have suffered much from dirt and neglect. . . . The series may be dated as having been painted between 1620 and 1630."

"William Harvey is shown as a man of about 45 [an age which he reached in 1623], with dark hair, a heavy moustache, and a small peaked beard. He is wearing a doublet. The background is inscribed, *Doctor William Harvey*. There is no date, but it is plain that we see here an image of Harvey as he was about 1620–1625 [that is, between the ages of 42 and 47], not long before he published his immortal treatise *De Motu Cordis* [1628]. The picture adds authenticity, if any were needed, to the later images already described,

[1] *The Portraiture of William Harvey*. By Geoffrey Keynes, M.A., M.D.Cantab., F.R.C.S. The Thomas Vicary Lecture, 1948. With a catalogue and reproductions of the pictures. (Pp. 42. No price.) London: Royal College of Surgeons.

since it was possible to recognize Harvey's face almost in the dark from knowledge of his appearance in old age."

It must indeed be a source of gratification to Mr. Keynes that he has been able thus to round off his account of the iconography of Harvey by the addition of a virtually unknown image painted many years earlier than any of those that have been described hitherto. We congratulate Mr. Keynes on this achievement of skill, pertinacity, learning, and special knowledge. And it will be a satisfaction to every medical man to know that he has here an honest picture of the greatest of all English medical men, represented as he was in the plenitude of his powers. It was painted before Harvey's fame had so risen that it provided a temptation to the artist to stylize his subject. We see at last the real Harvey as he appeared to his friends and family. It is to be hoped that adequate reproductions of this fine picture will be made available so that any English medical man may have upon his walls the inspiring image of his great progenitor.

CHARLES SINGER.

# Reports of Societies

## GENERAL PATHOLOGY OF VIRUS INFECTION

### PROFESSOR F. M. BURNET'S LECTURE

A special University of London lecture was delivered at the London School of Hygiene and Tropical Medicine by Professor F. M. BURNET, F.R.S. (University of Melbourne), on May 9. Professor Burnet is director of the Walter and Eliza Hall Institute of Research at Melbourne.

The general pathology of virus infection, said the lecturer at the outset, covered an enormous field, but he had chosen it because he felt that there was scope for the formulation of a simple framework of ideas. He had an impression that many people found difficulty in seeing the common features in the pathology of such simple virus diseases as measles, influenza, and herpes simplex. Amongst virus diseases there were those of short and of long incubation periods, some that conferred lifelong immunity, some, like trachoma, that persisted, and some, like herpes simplex, that recurred. He was looking for the common factors within this multiple behaviour.

#### Definition of a Virus

There was no universally accepted definition of a virus. The one he preferred was "a parasitic micro-organism considerably smaller than most bacteria, which is capable of multiplying only within living susceptible cells." That definition was elastic enough to permit the inclusion of rickettsia and the psittacosis group if they wanted them, and their exclusion if they did not. The time had passed, at least in the case of animal viruses, when it was necessary to qualify the statement that these were parasitic micro-organisms. It was some years since anybody seriously spoke of any of the animal viruses as non-living protein molecules.

The definition he had given limited virus growth to the interior of living cells. That restriction determined the general form of the technique which had to be used in experimental virology. Any virus disease of human beings or animals was initiated by a very small inoculum, perhaps involving in the first instance one or two cells only. If many more cells were involved symptoms appeared, and the patient recovered or died.

The process could be regarded (1) as it involved the individual cell, and (2) as it concerned the susceptible cells of the body as a whole. The entry of the virus into the cell, the intracellular multiplication, and the subsequent liberation of virus, associated usually with damage to the cell, must be considered; also, the process by which infection spread to other susceptible cells, and the process by which infection was overcome.

Professor Burnet said that he was compelled in an hour's lecture to treat each of these phases in a very summary and dogmatic fashion, but he felt sure that no listener would go away with the feeling that everything was known about virus disease. The matter he wanted to stress was the intracellular approach of the virus. His feeling was that one of the most interesting attacks on fundamental biological problems was being made at the present time with the use of viruses as "probes" to get into the inner functioning mechanisms of the cell. His hope was that out of this probing into the depths of the cell and the problems of cell infection and virus multiplication they might eventually come back to the hospital ward or the public health service with something worth while.

#### Entry into the Cell

To multiply intracellularly the virus must get into the cell. At the Walter and Eliza Hall Institute and at other centres the problem of the approach of the virus to the cell had engaged attention. There were several viruses which had no very restricted range of cells in which they could multiply. Vaccinia would multiply in a variety of cell types, psittacosis in an even wider range. Equally, there were a considerable number of types of cells within the body which had the capacity to take into their substance small foreign particles, whether virus or not, and he thought a fairly wide range of viruses, particularly those which entered the body through a traumatized area, appeared to be able to enter susceptible cells without any specialized mechanism.

Nevertheless, there were two groups of viruses in which well-marked invasion mechanisms had been elucidated. These were the bacterial viruses and the influenza virus. He would say nothing about the former, though actually the first work on the association of the virus and the surface of the susceptible cell was done with that group. The interest in the action of the virus on the cell surface was initiated by the discovery by G. W. Hirst in America in 1941 of the capacity of the influenza virus to agglutinate red cells. Influenza virus in the laboratory was grown in the allantoic cavity; it multiplied and was shed into the fluid. The first discovery was that red cells were agglutinated by the virus; the virus was adsorbed on to the cell surface, and it was actually the virus particles which were responsible for this agglutination of the red cells. That had recently been shown in work at Mill Hill on fowl red cells which had been exposed to virus.

The next discovery was the sequence of adsorption and elution. When red cells were mixed with virus adsorption took place, and the virus acted as a bridge which held the cells together. As they clumped the amount of free virus disappeared very rapidly. If this was left at 37° C. for an hour or two the agglutination would be found to have ceased. The interpretation was that the receptors which were present on the cells had been destroyed or changed, so that the cells were free to elute the virus. It would be realized that this essentially resembled an enzyme action. All these experiments were done with red cells, but further experiments showed that exactly the same phenomena could be observed in excised ferret lung.

These basic phenomena, the adsorption of the virus and its subsequent elution, had been the subject of a great deal of investigation. In the living animal the elution could not be demonstrated. The virus was taken up by the cells, apparently by the same mechanism, but it was not eluted; the process in the living cell went on to invasion.

The enzyme of the influenza viruses could be shown to be functionally identical with an enzyme secreted by the cholera vibrio. The use of this soluble enzyme had allowed a clear demonstration of the importance of adsorption of virus to all receptors in the initiation of infection. If a susceptible mouse or chick embryo were treated with this enzyme in sufficient concentration it was possible to protect against infection. With some viruses there was an extraordinarily protective effect. But unfortunately this work had no practical importance. The receptors very rapidly regenerated; indeed, a careful control of the experiment was necessary to get any results at all. There was no question about the reality of the results, but it was not a practical way of preventing the disease.

So far this work on the nature of the approach to the cell surface had been confined to the influenza group, which included, in addition to the influenza A and B viruses, the virus of mumps and that of the Newcastle disease of fowls. But there were suggestions that it might have a bearing on a number of other viruses. It appeared that one group of neurotropic viruses had the capacity to agglutinate red cells, and he

felt confident that when that was explored further a mechanism different from that of the influenza virus would be shown, but one equally relevant to the actual nature of virus infection.

His own (completely irresponsible) "hunch" was that in poliomyelitis it might be found that an attack along this line—observing how the virus got into a particular type of susceptible cell—would give results in the future. It was in the neurotropic group that advance would be made.

### Interior of the Cell

If one infected the chick embryo with a large amount of virus in the allantoic cavity, there was fair evidence that the virus particle entered one of the cells and that six or eight hours later something of the order of 50 to 100 descendent particles came out of that cell. With the bacterial virus much more accurate statements could be made. The problem was what happened between the entry of the virus particle into the cell and the liberation of 50 or 100 particles into the environment. There were a number of hints on what was happening; on the whole, nothing very definite could be said as yet, but it seemed to him that the nature of the activity of the virus within the cell might presently be made plain.

The suggestions found in experimental data of various sorts might be tabulated:

(1) The morphological changes which could be observed in the cell and which for many years had been described as inclusion bodies, cytoplasmic inclusions, and so on. That work must always be kept in mind, but at the moment there was a rather more dynamic approach to the problem, particularly with regard to the part played by the nucleic acids. It seemed fairly general that in the cells which could be conveniently examined there was a definite change associated with the early stage of virus infection, namely, an increase in ribonucleic acid. It was generally considered that this change indicated increased protein synthetic activity within the cell, and he thought that was a part of the puzzle which had to be fitted in.

(2) When virus entered the susceptible cell it disappeared, in the sense that when the membrane on which the virus had been placed was ground up nothing like the amount of virus which ought to be there could be demonstrated. There was some doubt about the significance of these findings. It might be that the virus was there, but blocked by something in the cells.

(3) Then there were the phenomena of interference. If, for example, mice were inoculated with a neurotropic strain of influenza virus they would die within five or six days, but if a small dose of that virus were mixed with a larger dose of non-neurotropic strain the addition would prevent the neurotropic or pathogenic strain from exhibiting its action, pointing very strongly to the likelihood that the interference was intracellular. Further study of this probable intracellular phenomenon might lead a long way.

(4) Another phenomenon which must not be forgotten was latency. Any sufferer from herpes of the lip would know that over long periods there was freedom from eruption, and then, apparently without cause, the eruption reappeared. The existence of these latent infections was a very important thing to be kept in mind when thinking what happened to the virus in the cell.

Some work had been done recently in Melbourne on the combination of the character of two viruses. Two strains of viruses, one neurotropic and the other non-neurotropic, were put into the mouse brain; afterwards, on grinding up the brain, one could with fair regularity get out a strain which was neurotropic but had the serological and immunological character of the second strain. The only explanation was that in some way the genetic qualities of two distinct virus particles had been combined or reunited. That interpretation was based to a considerable extent on the fact that with the bacterial virus this phenomenon had been worked out in some detail. He had no doubt that there was a combination of two different factors into what might legitimately be called a hybrid virus.

### Cellular Aspect of Virus Pathology

From all this body of evidence two pointers emerged. He put forward the hypothesis with reservation, but with a very strong feeling that it would turn out to be true. It seemed likely that when the virus particle entered the cell it disintegrated, perhaps under the action of a cellular enzyme, into a number of sub-units—perhaps between 100 and 500—small enough to come into intimate contact and association with those units within the cell which were responsible for the production of fresh cell substance, and which thus had their flow of energy directed not to the building up of the cells but to the replication in increasing amount of the virus units. As this switching of the metabolic process went on there was brought about a general disorganization of cell function, which at a certain stage began to break down. At this stage it might be assumed that the sub-units of the virus were reaggregated and the infective units were liberated.

There was a great deal more to be done before that hypothesis could be substantiated, but he thought it fair to say that the evidence from all the directions he had mentioned was compatible with such a hypothesis, and that it fitted in with the trend of modern thought among virus workers.

Professor Burnet said that he had spent a lot of time on this cellular aspect of virus pathology because he thought it had to be considered most deeply in an attempt to understand how viruses functioned. But before he left this part of the subject he would add that there was one thing which must be remembered: that even with the most active virus it was very rare indeed to find that all the cells which were susceptible to its action were destroyed. It was surprising when taking the fluid from a chick embryo with a high titre of virus in the fluid to find how many of the cells lining the cavity still looked perfectly normal when examined histologically. It had still to be discovered why a virus particle did not disorganize every cell it attacked. The question of interference might play a big part. It remained one of the difficulties of the virus worker to learn not why cells were destroyed but why so many which were subject to infection did not die.

### Ectromelia and Influenza

He would rely almost wholly on two groups of investigations which were carried out in the Walter and Eliza Hall Institute in Melbourne. There had been plenty of other work in other laboratories but these two did show something striking and provided a good start for an investigation of the problem of how the virus infections spread in the body.

Both these investigations made use of the laboratory mouse as a model of a human infection. In one the virus of ectromelia or mouse-pox was used, primarily because it was so closely related to the virus of smallpox. The virus particles were the same size as in those of smallpox, were of almost identical serological character, and in all major qualities (except their range of pathogenicity for different species) they were similar. Protection from both these diseases was given by ordinary Jennerian vaccination.

Mouse-pox was picked up in nature by contact of the animal with infected bedding, and the virus got in through a small abrasion which was the primary lesion. If the mouse had been naturally infected and did not die at once there would be found after eight to ten days on depilating the animal a characteristic rash which in all essential details was equivalent to the rash of smallpox, merely modified by the much thinner character of the mouse skin. The interpretation made by F. Fenner in Melbourne, based on titration of virus in various organs at various times, was that after a small skin lesion the virus multiplied and spread to the lymph nodes and into the blood stream. This primary viremia allowed the virus to pass to the spleen and liver and it might well concentrate there. If the concentration was extremely high the mouse died with necrosis of liver. But much greater amounts of virus were liberated into the blood stream, and infection of the skin took place at this period. Up to this point there had been virtually no symptoms or signs. By about the seventh day the primary lesion had spread to give a visible swelling of the foot, by the ninth day papules appeared in the skin, and by the eleventh day there was ulceration and severe rash. That was the general story that Fenner obtained in his study of mouse-pox. Mouse-pox had the capacity of multiplying in a fairly wide range of cells.

The other Melbourne investigation was in process of being published. It was carried out on the same lines, but with an entirely different virus—that of influenza. It was started with the object of finding out as much as possible what happened in the mouse lung, with techniques involving the use of mouse lung *in vitro*. It was found, as might be expected, that with influenza virus the whole process was a surface one. The

susceptible cells were those lining the surface of the respiratory tract.

The findings suggested that when a small inoculum of influenza virus was given intranasally (that was, essentially, intratracheally in the mouse) a few cells became infected on the epithelium lining one of the bronchioles, multiplication took place, a second generation of virus particles were liberated and were swept upwards by the forces at work in the tubules (the ciliary movement being almost entirely upwards) and lesions were produced in the mouse lung. The susceptible cells were those lining the respiratory tract. There was no opportunity for distant multiplication, though with another virus—that of mumps, which was distinctly similar to influenza—manifestations were shown in the pancreas and in the salivary glands.

One of the outstanding things to be found out about some of the virus diseases was the nature of the primary initiating infection. There were two diseases in which such investigation should be particularly carried out—smallpox and mumps. In both, the virus was manipulable in the laboratory, and there was a big field of work here. A concentrated attempt should be made to understand human smallpox, and Fenner's work afforded a good pointer.

### Recovery and Immunity

In conclusion, the lecturer turned to the process of recovery and immunity. He thought that despite the enormous complexity of this subject in relation to virus diseases there were one or two generalizations which could be made with some confidence and would be helpful to people trying to understand the general picture of virus disease. Frequently one found pathologists who were dubious about the importance of the antibody. There was a tendency to scoff at antibodies, particularly antibodies shown only by aggregation reactions in test-tubes. It must be realized that when antibody was spoken of in virus work, with few exceptions the antibody was determined in blood or serum by the direct functional test of mixing the serum with certain amounts of virus and showing that that mixture did not infect susceptible cells.

In approaching immunology it might be a good thing to start with a discussion of the situation in a typical virus disease such as yellow fever. All surveys of yellow fever in Africa or elsewhere were based essentially on the detection of a circulating antibody. There was one generalization which could be made at this point: any antibody in the organism was effective in so far as it could come into effective contact with the virus particles before such particles entered the susceptible cell. In yellow fever the immunity was extraordinarily effective and long lasting. A very strong stimulation to antibody production might be given, and the antibody remained circulating for years.

Some interesting observations had been made on what determined the resistance of the mouse in withstanding the challenge of active virus. Two groups of mice which had been immunized by intraperitoneal inoculation against influenza A were taken, and to one group an influenza B vaccine was given intranasally. Influenza B vaccine in itself had no protective effect whatsoever against influenza A; nevertheless, this extra manipulation enormously increased the resistance of those mice to influenza A. What had happened was that by giving the intranasal vaccine the antibody produced by the intraperitoneal vaccine was enabled to pass more freely from the blood vessels in the lung to the bronchial surface. The effective place for the action of the antibody in influenza was in the film of fluid which lay over the susceptible cells. Here was probably to be found the explanation of the difference between the long-lasting immunity in yellow fever and the short-lasting immunity in influenza.

In herpes of the lip there were always plenty of antibodies in the circulating blood, and yet the eruption had a tendency to reappear. This was because the virus was in the cell, and entirely immune from the action of the antibody. In the cell it multiplied, and only with the breaking-down did it come in contact with the antibody, so that the eruption once again cleared up.

The whole story of immunity in virus disease was essentially related to the circulating antibody, the degree to which it was produced, and the effectiveness with which it was brought to the virus before the virus reached the stage of infecting large numbers of susceptible cells.

"I have had to hurry over a large field," said Professor Burnet, ending his lecture, "but I hope I have shown that there are certain generalizations which may be helpful in understanding this subject. Virus infection is essentially an intracellular process. For some, but not all, viruses there is a rather elaborate mechanism for coming into contact with and passing through the cell membrane. The multiplication of the virus within the cell is in all probability a more complex process than binary fission. The spread of infection is determined, first, by the range of cells which are susceptible to viral infection, and, secondly, by simple anatomical relationships of those cells with regard to the blood stream and so on. Finally, recovery and immunity are predominantly determined by the production of antibody, and the effectiveness of the antibody will be determined by the concentration in which it is present and its ability to block the virus before extension to susceptible cells can occur."

The lecture, at which Professor Wilson Smith presided, was given to a crowded theatre. A vote of thanks was accorded to the lecturer on the motion of Dr. C. H. Andrewes.

---

## ACUTE TUBULAR NECROSIS

At a meeting of the Section of Experimental Medicine of the Royal Society of Medicine on May 9 three papers were read on aspects of acute tubular necrosis. The President (Professor G. W. PICKERING) said that this type of lesion was first observed during the war, when workers at the Hammersmith Hospital noticed that the air-raid casualties who developed uraemia were those in which there had been crushing for long periods. A similar condition was very common after abdominal wounds.

### The Renal Lesion

Professor J. H. DIBLE remarked that in the study of acute tubular necrosis an immediate difficulty was that such patients generally lived six to eight days, and it was not easy to say whether people who had died within a few hours or days of some other cause would have developed the characteristic lesion; there were certain indications, such as the presence of anuria or (in the case of pigment nephroses) of pigment in the plasma, that had they lived they would have done so.

The first illustration which Professor Dible showed was of the kidney of a man who died 20 hours after crushing. The kidney was normal in almost every respect. There was congestion of both cortex and medulla, and what appeared to be the beginning of the characteristic lesion could be observed. It began in Henle's tubules, more especially in the intermediate zone, and there was evidence that it involved especially the ascending limb and second convoluted tubule. The fully developed lesion appeared after a couple of days. There was granular material in the glomerular space and sometimes some overgrowth of the capsular cells. The first convoluted tubules contained debris, and, in the case of myohaemoglobin or haemolytic syndrome, pigmented material was present especially in the second convoluted tubules. The lesion appeared to affect the whole nephron. There was evidence of cellular necrosis. Whatever the cause of the tubular necrosis, the cast material which appeared in the second convoluted tubules in the early stages was hyaline and non-pigmented; where pigment was present it appeared at about the second day; it was sometimes in long strands, sometimes it formed a lining to the tubule, and sometimes it was an amorphous granular mass.

In the boundary zone, areas of cellular infiltration and inflammation were marked about the fifth or sixth day. These foci of necrosis were characteristic, as were the so-called "tubulo-venous lesions," which had a similar aetiology.

At a later stage the acuteness of the process regressed, and there appeared what was in effect a small area of fibrosis on what one assumed was the site of the acute tubular necrosis. A difficulty which had to be borne in mind, particularly in the

case of elderly patients, was that this fibrotic appearance was seen in any disease of the nephron.

Summarizing the changes observed, Professor Dible said that up to 30 hours the kidney appeared congested and the cortex full of blood. After that time the cortex was relatively bloodless. In about 30 hours casts began to appear, but whatever the cause of the condition these did not show pigmentation until about 40–48 hours. Inflammatory changes took place four to six days after the injury. It seemed that the pigmentation in the haemolytic conditions was a secondary development and not essential to the process, though the lesions tended to be more severe where pigment was present. This was probably due to the added poisonous action of the pigment itself. The inflammatory changes were clearly secondary to the earlier necrotic ones.

Professor Dible divided cases of acute tubular necrosis into those with pigmentation and those without, the former including necrosis following transfusion, the presence of myohaemoglobin in the circulation, blackwater fever, quinine poisoning, certain cases of abortion, and obstructive jaundice. The latter followed shock with low blood pressure (with or without haemorrhage), burns, and acute septicaemia. Similar lesions had been seen in cases of acute streptococcal infection, in sulphathiazole poisoning, following stilboestrol therapy, in pelvic sepsis, and to some extent in hydronephrosis. In all these cases the lesion was of the same pattern, and although it varied a good deal from case to case there was a common picture of tubular necrosis.

### Functional Pattern

Dr. G. M. BULL said that the functional pattern of acute tubular nephrosis, equally with the pathological picture described by Professor Dible, was characteristic and uniform. He presented the data from 34 of 100 patients with anuria, of whom about half were suffering from acute tubular nephrosis; they had been investigated by Dr. A. M. Joekes, Dr. K. G. Lowe, and himself. A striking feature was the uniformity of functional pattern despite the widely varying causes, ranging from pure poisoning to "shock kidney." He divided the clinical course of the illness into an onset phase, lasting from a few minutes up to some hours or occasionally days, an oliguric or anuric phase during which the blood urea mounted, an early diuretic phase, and a late diuretic phase.

The first group of tests carried out related to tubular function. The normal kidney concentrated the urea or creatinine to many times its level in the blood, particularly at low rates of urine flow. The ratio of the urine concentration of creatinine or urea to that in the plasma could be used as an index of tubular function; if the tubules were inactive, glomerular filtrate would appear in the urine and the ratios would be 1 : 1. The ratios fell rapidly towards unity and returned well after the onset of diuresis.

Normally, a low concentration of sodium, chloride, or potassium ions in the blood was associated with such active tubular resorption of the ions that the urine contained less than many samples of tap water. This capacity of the tubules to recover salts from the glomerular filtrate could be expressed in a ratio of plasma over urine concentrations. The mean plasma/urine concentration ratios for sodium and chloride in the patients in whom the point could be examined were 2:1, and there was a delay between the onset of diuresis and return of tubular function. This delay was on an average as long as the preceding period of anuria or oliguria. As an index of tubular function these ratios were valid only when there was a body need for the ions. The resorption of sodium, chloride, and potassium were all affected, and losses of these minerals in the early diuretic phase were of great importance in treatment.

The renal extraction of para-amino-hippurate was found to be low compared with the normal; this, and the results of other tubular function investigations, confirmed a general dysfunction.

Investigations showed very low rates of renal blood flow and a high arterio-venous oxygen difference, so excluding the operation of an "Oxford shunt" in the oliguric and diuretic phases of the illness. The rate of cardiac output was found to be within normal limits, and in the properly treated patient no disturbance of circulation other than in the kidney was found. Eight of the patients had splanchnic block or spinal analgesia, and in no case did these procedures appear to alter the course of the illness.

In some cases tubular dysfunction was probably the result of toxic damage alone; in others of primary ischaemia only. This primary ischaemia might result from prolonged severe hypotension or from reflex or humorally induced renal vasoconstriction, or even from an "Oxford shunt." A second point of interest was the cause of the secondary diminution of renal blood flow. It did not respond like the primary ischaemia to the correction of extrarenal factors. It was not a shunt, because it did not respond to splanchnic block, because the renal venous blood was more venous than normal, and because the rate of blood flow was far lower than occurred in experimentally induced shunts. It was not the result of any other neurogenic mechanism. One was forced to conclude that it arose because of some local and mechanical factor in the kidney.

Finally, Dr. Bull put forward the view that chronic forms of tubular nephrosis existed. Any sufficiently severe attack left its scar on the kidney, and recurrent attacks probably led to a contracted kidney. The contracted "alkalotic" kidney might be an example of this process.

### Aetiology

Dr. E. M. DARMADY discussed the aetiology of acute tubular necrosis. He divided the cases into seven groups: (1) Shock following accidents, gunshot wounds, and certain operations; (2) cases associated with disturbance of water and/or electrolyte balance, as in acidosis and alkalosis, or diabetic coma, diarrhoea, and pyloric stenosis; (3) cases associated with intravascular haemolysis following shock and/or excessive loss of fluid or salt, as in crush syndrome, incompatible blood transfusion, blackwater fever, and after myanesin; (4) allergic reactions such as favism, sulphanilamide anurias, and streptomycin and penicillin sensitivity; (5) cases in which the acute uraemia is associated with known nephrotoxins; (6) cases with either systemic infections, such as pneumococcal pneumonia, typhus, or Weil's disease, or localized ascending infection, such as pyelonephritis and infection following prostatectomy; (7) those associated with obstetrical conditions, protein depletions, and water intoxications.

There was considerable overlapping between the groups, and in determining the aetiological factors responsible it was sometimes difficult to ascertain the main group. The clinical course of many of the conditions was so similar that one wondered whether they arose as a single pathological entity, and there was some support for that view.

The theory that renal failure was due to blockage of the tubules by pigment casts could no longer be accepted. Using the technique developed by Professor Jean Oliver, of Long Island, whereby the nephron could be dissected out whole after maceration of the kidney with acid, it was possible to examine the nephron throughout its course, and Dr. Darmady showed photographs of such dissections.

In two portions of tubules shown there was no evidence of dilatation above, and the composition of the casts appeared to vary throughout their length. The casts tended to form in single nephrons, while other nephrons appeared to be free. These appearances in the nephron could be explained by supposing dirty water being allowed to flow through a pipe—afterwards the sludge would be found to form small collections of deposits in the manner of these casts. If this method of cast formation was true, remarked Dr. Darmady, damage to the nephron in its course would be expected, and he showed slides of dissected nephrons revealing such damage. If pigment casts were toxic, lesions would occur at points adjacent to the formation of the casts, with the exception of cases due to chemical nephrotoxins.

It would seem that neurogenic stimulation causing renal vasoconstriction could account for only a proportion of cases. In a recent experiment at the Johns Hopkins Hospital dogs had their spinal cord cut and the renal nerve supply divided; a tourniquet was applied to a hind limb for four hours, and this was followed by oliguria in the usual manner. The suggestion was that something other than the nerve supply controlled the renal system. In looking for some other

controlling mechanism the possibility that the alarm syndrome of Hans Selye might be a factor seemed worthy of further consideration. Some confirmation of this could be obtained from the fact that many operations were followed by renal failure and acute uraemia.

Finally, Dr. Darmady suggested that "lower nephron nephrosis" was not a suitable name for the kidney changes found in acute tubular necrosis.

## MICRO-WAVE THERAPY

At a meeting of the Section of Physical Medicine of the Royal Society of Medicine on May 10 Dr. FRANK H. KRUSEN (Mayo Clinic) delivered the Samuel Hyde Lecture, taking as his theme "Micro-wave Therapy."

Dr. Krusen said that for many years electric currents of high frequency had played an important role in medicine and surgery, until diathermy of one million or more cycles per second had been obtained. Micro-wave therapy, however, employed frequencies of from one thousand mega-cycles per second upwards. The experiments on tubes of large enough wattage to provide radiation for medical use were held up by the war, and before the war suitable generators of micro-waves did not exist. In 1946, however, the lecturer found what he had been looking for, and the Massachusetts Institute of Technology furnished a micro-wave generator with an output of 4,000 watts and a frequency of 3,000 mega-cycles per second on a wavelength of 10 cm., and thereupon the studies of micro-wave therapy began.

Experiments on animals quickly showed that micro-waves could heat deep tissues satisfactorily, also that the maintenance of the temperature in the deeper tissues was longer than in the superficial ones. It was also found by experiments with directing appliances that micro-wave therapy furnished a means of heating tissues with much more accurate localization, the beam of energy being directed upon the part as desired, and that the absorption of the energy so directed was greater than with longer wavelengths. The possibility of placing the director in any position gave great flexibility in the treatment. There was no evidence of burning in these first experiments, but it was afterwards shown that the length of exposure, and not the height of the temperature alone, was a factor in any burning of the tissues. Micro-wave diathermy must be employed with caution in any parts of the body where there were bony prominences or collections of fluid, or where any metal had been inserted. The average increase in temperature obtained in bone exposed for 30 minutes, with muscles and other tissues lying between the bone and the source of energy, was 4.3° C. The effect of exposure on the eyes was studied in animals, and it was found that at certain intensities corneal clouding and cataract developed. Evidently micro-wave therapy should be applied with extreme caution in the region of the eye, but the eye could readily be screened from the radiation.

Fifty volunteers were next taken as the subject of experiment. It was found that the average increase in the temperature in muscle was greater than in the subcutaneous tissue, and the increase in the subcutaneous tissue was greater than in the skin. After 20 minutes' exposure the flow of blood continued to increase, and reached its height at 30 minutes. The effect having been established, clinical treatment was started on a selected group of patients. Altogether 481 patients had so far received treatment. The great majority (368) had been treated for shoulder lesions, but the method had also been used for fibrositis elsewhere and other conditions. Of those treated for shoulder lesions, 286 had been traced, and of these 28% showed excellent improvement, 43% good improvement, 24% slight improvement, and 4% no improvement. The results compared favourably with those obtained by short-wave diathermy. Untoward symptoms were noted in only 3.2%; one patient suffered a first-degree burn. Sixteen of the patients had been treated, at different times, by micro-wave and short-wave diathermy, and nine of them reported that they preferred the former because there was less systemic heating, less perspiration, and no weight or pressure from the applicator, and yet adequate local heating was obtained.

Dr. Krusen thought it might be concluded that, while more clinical investigation must be carried out before the exact place of micro-wave diathermy in clinical practice could be estimated, and certain precautions must be taken, it offered considerable advantages. Like all forms of heating which were employed therapeutically, it had certain shortcomings. Tissues might be damaged by excessive doses. Ischaemic tissues and tissues containing large amounts of fluid might suffer from excessive heating, and care must be taken in the region of the eye, in parts with bony prominences, and in tissues containing metal bodies. In spite of all this, micro-wave diathermy had a number of advantages over the ordinary methods of applying heat locally to living tissues. It provided a new and extremely flexible and effective means of heating living tissues, permitting accurate localization by direction of a beam of energy to any surface of the body. There were greater rises of temperature in deep muscle when micro-wave diathermy was employed, and a desirable relationship was established between the outer and internal temperatures. Its proper application would produce readily controlled increases of temperature in subcutaneous tissues, muscle, deep fascia, and bone and bone marrow. By the use of an impedance matching transformer the amount of energy entering the skin was increased, there was less refraction, and therefore higher temperatures were obtained to a depth of 2 cm.

Dr. P. BAUWENS, speaking on a vote of thanks to the lecturer, said that it seemed to him that if micro-wave therapy could be compared with anything it should not be with ordinary diathermy but with the use of infra-red rays and possibly some radiations in the visible spectrum which they knew were deeply absorbed.

## BRITISH ORTHOPAEDIC ASSOCIATION

The spring meeting of the British Orthopaedic Association was held in Cardiff on April 21 and 22 under the presidency of Mr. S. L. HIGGS. Papers were presented in the Reardon-Smith lecture theatre of the National Museum of Wales, and clinical cases were shown at the Cardiff Royal Infirmary.

### End-results of Fracture of the Patella

Mr. J. TODD (Newcastle-upon-Tyne) reviewed the results of 46 cases of fracture of the patella, 16 of which were treated by suture with catgut and 30 by excision. Good or excellent results—judged by function, movement, and capacity for work—were gained in 68% of the cases treated by suture and in 80% of those treated by excision. In general, movement was slightly better after excision, but power was better after suture. Mr. K. H. PRIDIE (Bristol) advocated repair of transverse fractures by a single vertical screw. This afforded better apposition and fixation than suture with catgut and allowed immediate movement.

Mr. D. L. SAVILL (Edinburgh) had studied the condition of the manubrio-sternal synchondrosis in 61 cases of ankylosing spondylitis, and had found evidence of pathological changes in 72%. Radiographically the joint was shown best by a lateral projection. When the joint was affected in ankylosing spondylitis there was progressive narrowing of the cartilage and erosion of the bone ends. The process was limited by a narrow zone of sclerosis, and the joint line was increased in depth antero-posteriorly. In the later stages the joint was obliterated completely by bony ankylosis. These changes were essentially similar to those occurring in the sacro-iliac joints.

Mr. A. C. BINGOLD (Leeds) showed radiographs of five patients in whom the bones in the region of the hip-joint were affected by fibrous dysplasia of the monostotic or polyostotic type.

Mr. BRYAN MCFARLAND (Liverpool) discussed the results in nine cases of pseudarthrosis of the tibia treated by the "by-pass" bone-grafting operation described by him in 1938. He recalled the essential features of the operation, which consisted in placing a cortical graft as a strut to bridge the pseudarthrosis—without correction of the anterior angulation—the ends of the graft being locked into notches cut in the upper and lower fragments. The strut resisted the bending stresses acting

at the site of fracture. The operation had been successful in securing bony union in seven patients, and unsuccessful in two; failure was probably caused by technical errors. Pseudarthrosis of the tibia was neither a birth fracture nor a non-fusion of two separate centres of ossification—it was a stress fracture in a tibia that was congenitally abnormal. The abnormality occurred in the mesenchyme, and might give rise to a cyst or to an area of slender bone of inadequate strength. Pseudarthrosis had been produced experimentally in chickens by injecting insulin into the embryo at the appropriate period of development.

### Operations on the Hip

Mr. R. C. HOWARD (Norwich) described a method of arthrodesis of the hip (developed in association with Mr. H. A. Brittain) in which fixation of the joint by a nail was combined with ischio-femoral grafting. The bed for the graft was prepared by passing a wide-diameter drill through the upper part of the femoral shaft into the ischium. The nail and the graft formed a V, which made for mechanical rigidity. Prolonged immobilization in plaster was unnecessary, and walking with crutches was permissible within a few weeks of the operation. The main indication for the operation was unilateral osteoarthritis of the hip. Sound bony fusion had been secured in 14 of 17 patients operated upon.

Mr. G. V. OSBORNE (Liverpool) reviewed 75 patients in whom oblique displacement osteotomy of the femur had been performed for osteoarthritis of the hip. The most suitable patients were those with gross osteoarthritis and fixed adduction deformity; the operation should be avoided when a free range of abduction remained, and when marked flexion deformity could not be corrected by preliminary manipulation. The mechanical disadvantage of the hip—due to leverage factors—was such that the thrust through the joint was equal to at least twice the weight of the body, and considerably more when adduction deformity was present. Displacement osteotomy overcame this mechanical disadvantage. It reduced leverage by bringing the line of body weight near to the axis of the femoral shaft and by affording a bony block to prevent adduction. The operation had been successful in relieving pain and restoring adequate function in 61 cases, and unsuccessful in 14. Many of the failures were attributable to errors of technique.

Mr. R. G. TAYLOR (Oxford) studied the late results in 93 patients treated for osteoarthritis of the hip, ankylosing spondylitis, and other conditions by excision of the head and neck of the femur. The results were good in 83 cases and poor in seven cases. Three patients died as a result of the operation. In successful cases the operation relieved pain, corrected deformity, and restored free movement.

Discussing the three preceding papers, Mr. H. A. BRITTAIN (Norwich) conceded that the best results of arthroplasty were better than those of arthrodesis. But the results of arthroplasty were often bad; arthrodesis was more reliable. Mr. A. LAW (London) believed that there was not, and never would be, a universal operation for osteoarthritis of the hip. The treatment of every case must be decided on its merits. Mr. O. VAUGHAN-JACKSON (London) said that any method of arthrodesis in which external fixation was omitted would stand or fall by the efficiency of the internal fixation. The efficiency of nail fixation was greatest when the nail was placed eccentrically rather than centrally in the femoral neck. Mr. NORMAN CAPENER (Exeter) emphasized the merits of the posterior approach to the hip-joint. He could not agree with those who stated that cup arthroplasty was a more formidable operation than pseudarthrosis.

### Treatment of Volkmann's Contracture

Mr. A. R. PARKES (Glasgow) had treated two patients with established Volkmann's contracture by tendon transplantation designed to restore independent action to the flexor digitorum profundus tendons without interfering with active movement at the wrist. He recalled that by the use of flexion-extension movements of the wrist many patients were able to move the fingers through a limited range, despite the loss of independent action of the finger flexors. It was unwise to sacrifice these trick movements by arthrodesis of the wrist, which had sometimes been advised in conjunction with tendon transplantation. The operation he had used consisted in division of the contracted finger flexors (sublimis and profundus), division of contracted wrist flexors, and transfer of extensor carpi radialis longus to the distal stumps of the profundus tendons above the transverse carpal ligaments. The operation had given promising results. Mr. D. Ll. GRIFFITHS (Manchester) recalled that the extensor muscles were often affected in Volkmann's ischaemia. It was necessary to be quite certain that there was adequate voluntary power in the wrist dorsiflexors before undertaking this operation. Mr. H. J. SEDDON (London) hoped that the operation might reduce the indications for prolonged stretching of the contracted tissues, and for such operations as shortening of the forearm bones. The muscles affected most seriously by ischaemia were the flexor digitorum profundus and flexor pollicis longus. Involvement of the superficial flexors was often relatively slight, and their action could be adequately reinforced by transplants. Arthrodesis of the wrist made available sufficient extensor tendons for transfer to flexor pollicis longus as well as to the finger flexors.

Dr. G. N. C. CRAWFORD (Oxford) had placed multiple indian ink marks along the length of suitable tendons of growing rabbits and had measured the intervals between the marks. The same intervals were measured again after killing the rabbits three to four months later. Growth of tendon occurred interstitially throughout its length. The most rapid growth was near the muscle–tendon junction.

### Amputations for Vascular Disease

Mr. HARMAN SMITH (London) had examined 138 amputation stumps in 95 patients with primary vascular disease of the lower limbs. The object of his investigation had been to assess the criteria that could be relied upon to determine whether below-knee amputation was likely to be adequate. The most significant factors were age, the state of the popliteal pulse, and the amount of bleeding at operation. When bleeding was sluggish and the muscles grey, amputation at a higher level was indicated, but when free bleeding occurred from healthy muscles a satisfactory stump could be anticipated.

Mr. JOHN CHARNLEY (Manchester) showed histological sections taken from the line of arthrodesis at various intervals after "compression" arthrodesis of the knee. He demonstrated convincingly that the line of fusion was bridged by trabeculae of woven bone as early as four weeks after operation. At eight weeks healing by fully established woven bone was almost mature. It was still uncertain whether this rapid bony union was determined by pressure or simply by close apposition of the fragments.

Mr. J. H. PENROSE (Bristol) reported seven cases of Monteggia fracture with posterior dislocation of the radial head. He considered that the mechanism of the injury was similar to that which caused posterior dislocation of the elbow—a fall on the hand, the elbow being slightly flexed and the forearm in moderate pronation. In every case there was a marginal fracture of the head of the radius. Treatment was by intramedullary fixation of the ulna and excision of the radial head or of the detached fragment. All patients regained good function but some limitation of elbow movements was usual. Mr. E. MERVYN EVANS (Birmingham) agreed that the injury was closely related to posterior dislocation of the elbow. He felt that closed manipulation—by full extension and supination—should be tried before open operation was resorted to.

Mr. E. SHEPHARD (London) had observed the movements of the tarsal joints in living and dead feet. Only two movements were possible: supination (combined inversion and adduction) and pronation (combined eversion and abduction). These movements might take place at the peritalar joint or at the mid-tarsal joint. The peritalar joint comprised the talonavicular joint and the sub-taloid joint. Its mechanism was comparable to that of the radio-ulnar joints. The peritalar joint allowed a wide range of supination and pronation about an axis directed obliquely downwards and backwards through the body of the talus. The mid-tarsal joint allowed a small range of supination and pronation about a similar axis.

Mr. DAVID THOMAS (Scunthorpe) presented an analysis of 109 stable fractures of the lateral malleolus, 59 treated by immobilization in plaster and 50 by simple strapping. The average period of incapacity was eleven and a half weeks for patients treated in plaster, and only six weeks for patients treated by strapping. The slower rate of recovery with the plaster method was probably due to loss of the normal pump action of the muscles (and consequent oedema) while in plaster and to interruption of the normal walking habit. Mr. H. OSMOND-CLARKE (London) said that if these fractures were to be treated by strapping it was necessary to be quite sure that the fracture was stable. Mr. V. H. ELLIS (London) doubted whether working time was saved by avoiding plaster. Many patients were able to return to work in plaster who otherwise would be unwilling to do so because of pain. Mr. P. H. WILES (London) and Mr. W. D. COLTART (London) favoured plaster immobilization.

# Preparations and Appliances

## A NEW TYPE OF FOOT SUPPORT FOR THE LITHOTOMY POSITION

Mr. G. E. E. USHER-SOMERS, resident obstetric officer, Hallam Hospital, West Bromwich, writes: The apparatus here illustrated consists of two foot-rests made in the form of sandals which support the feet in a position of external rotation and inversion. The rests are attached to the sides of the operating table or labour-ward bed, and are adjustable to the length of the patient's leg. The angle of inversion and the distance between the feet are the factors in determining the amount of abduction of the thighs, and when this is correct the patient's knees fall naturally apart without any tendency to over-abduction or strain on the hip-joint, either with the conscious or the anaesthetized patient. The most important adjustment is that of approximation of the feet, thus accommodating the apparatus to varying lengths of leg: in practice this is required only when there is a marked difference in the stature of the patients. This adjustment is made by a simple sliding bar and socket, which is self-locking. The foot-rests have also been adapted to fit any operating table, and are now used continually for gynaecological operations, cystoscopies, and haemorrhoidectomies.

FIG. 1.—One of the foot rests.

FIG. 2.—Photograph taken after delivery; showing good abduction of thighs and easy access to perineum.

The apparatus has been in use for six months in the Maternity Department of this hospital with complete satisfaction. It has been used for forceps deliveries under general anaesthesia and also for normal deliveries and suturing of the perineum under local analgesia. The patient is far more comfortable than with the old type of stirrup, and exposure is good. There is no pressure on any part of the leg, thus avoiding a possible source of venous thrombosis, which is thought to occur from pressure of the upright bar on the inner side of the calf.

I attach great importance to the fact that the nursing staff, who at first were very sceptical about the new apparatus, very soon changed their opinion, and now definitely prefer it for its simplicity and adaptability.

# Correspondence

## Intestinal Obstruction Due to Food

SIR,—Mr. Neil Ward-McQuaid's article on "intestinal obstruction due to food" (May 13, p. 1106) reminds me of an incident which occurred some 12 or 15 years ago at St. Bartholomew's Hospital and enables me to add one more to the recorded list of foodstuffs causing obstruction. The scene was an operating theatre at midnight, the patient a small boy of 9 or 10, the season about December 27. The boy presented every sign of acute intestinal obstruction, and I performed a laparotomy in the expectation of finding a "band" or one of the other more usual causes of obstruction. Instead it was found that the terminal four or five inches of the ileum was packed with a solid mass of food. Through the thin, purplish wall of the paralysed and distended gut it was possible to recognize all the ingredients of what must have been a very satisfactory Christmas pudding. The pultaceous mass was gently milked through the ileo-caecal valve into the caecum, and the boy made a very good recovery.—I am, etc.,

London, W.1. GEOFFREY KEYNES.

SIR,—The article by Mr. Neil Ward-McQuaid (May 13, p. 1106) and a previous one by Mr. A. Lyall[1] describing acute intestinal obstruction from undigested food make no reference to a short paper of mine published in 1924 describing two cases of acute intestinal obstruction due respectively to a fig and a raisin.[2] Since the publication of that paper I have had (in 1927) a further experience of obstruction in a boy aged 11, due to the impaction of a large mass of peanuts and coconut in the rectum.

This boy had consumed a very large quantity, probably over a pound, of nuts three days previous to my seeing him, and his doctor was called in because of severe tenesmus and the passage of streaks of blood from the bowel. On examination, the rectum was completely filled with a mass of nuts, spherical in shape and about 6 in. (15 cm.) in diameter. The abdomen was slightly distended, ladder patterns of small intestine were seen, and there was much gurgling on palpation. Under a general anaesthetic the rectal sphincter was stretched and the mass removed digitally and with a spoon, the quantity of nuts being so great that it filled a third of a large chamber-pot. Faecal matter was then felt and flatus passed. An enema on the following day gave a good result, mainly of faeces with a few portions of nut. The patient is alive and well and is now a responsible business man.

—I am, etc.,

Dundee. R. CHARLES ALEXANDER.

REFERENCES

*British Medical Journal*, 1945, **1**, 734.
[2] *Edinb. med. J.*, 1924, **31** (n.s.), 617.

SIR,—Mr. N. Ward-McQuaid (May 13, p. 1106) does not mention tomato skin in his very comprehensive list of obstructive foods. Some time ago I examined a lady, aged 65 years, edentulous, who had intestinal obstruction by a "foreign body" (40 by 30 by 30 mm.) situated four feet above the ileo-caecal valve. On inspection this "foreign body" appeared to be an artichoke; later, after maceration in formol saline, the "body" was shown to be a mass of tightly rolled skins from segments of tomatoes, cemented firmly together by hard, brown faecal material which on prolonged soaking became a brown sludge. It was thought that the bolus must have been built up slowly over many days or weeks. The condition was not diagnosed during life, the patient being admitted to hospital in coma and *in extremis*. Another interesting case was a baby who swallowed a rubber teat from an ordinary feeding-bottle, a number of these rubber teats having been included among his ordinary playthings.—I am, etc.,

Epping, Essex. FRANK MARSH.

## Age at the Menarche

SIR,—In view of Professor R. W. B. Ellis's paper (January 14, p. 85) showing that puberty occurs later in Nigeria than in this country, the following observations on the age of the menarche in Ceylon may be of interest. They were made by one of us (D. C. W.) in February and March, 1950, in the course of an investigation on endemic goitre on behalf of the World Health Organization.

Information was obtained from 1,140 Ceylonese girls between the ages of 10 and 20 years. Of these 844 were at school in Colombo; the remainder were at rural schools. Each girl was asked her present age in years and months and whether her menstrual periods had started. With the aid of the standard statistical technique of probit analysis the average age of attainment of the menarche can be determined from these data alone without having to rely upon the girl's memory of her age at the onset of menstruation.

TABLE I.—*Age of Attainment of the Menarche in Ceylon, Nigeria, and the South of England*

| Group | No. of Children | Mean Age of the Menarche (Years) | Standard Error of the Mean | Standard Deviation of Age of the Menarche (Years) | Coefficient of Variation (per cent) |
|---|---|---|---|---|---|
| Ceylon Urban .. | 844 | 12·84 | ±0·07 | 1·24 | 9·7 |
| Ceylon Rural .. | 296 | 14·39 | ±0·16 | 1·73 | 12·0 |
| South of England .. | 2,590 | 13·49 | ±0·04 | 1·19 | 8·8 |
| Nigeria (Ellis, 1950) | 300 | 14·22 | | 1·00 | 7·0 |

The results of the analysis are presented in Table I. The first point of interest is the considerable difference in average age of the menarche in Ceylon between the urban girls (12 years 10 months) and the rural girls (14 years 5 months), which is statistically significant. The age of attainment of the menarche is not only later on an average but also more variable among the rural than among the urban Ceylonese. The standard deviation is 1.73 years for rural and 1.24 for urban girls—again a significant difference. The respective coefficients of variation are 12.0% and 9.7%. Table I also contains a comparison between the Ceylon figures, those given by Prof. Ellis for Nigeria, and the findings for 2,590 day-school girls in the south of England (to be published later). The Nigerian girls correspond closely in mean age at the menarche to the rural Ceylonese, but show considerably less variation, the respective standard deviations being 1.0 and 1.7 years. The mean age of the menarche in the English girls lies between those for the urban and rural Ceylonese, and differs significantly from each. These English girls, however, showed no urban–rural difference.

TABLE II.—*The Ages by which Certain Percentages of Girls have Attained the Menarche in Ceylon, Nigeria, and England*

| Percentage who have Attained the Menarche | Ages for | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Ceylon Urban | | Ceylon Rural | | South of England | | Nigeria | |
| | Years | Months | Years | Months | Years | Months | Years | Months |
| 1% | 9 | 11 | 10 | 4 | 10 | 9 | 11 | 11 |
| 50% | 12 | 10 | 14 | 5 | 13 | 6 | 14 | 3 |
| 99% | 15 | 9 | 18 | 5 | 16 | 3 | 16 | 7 |

Table II shows these differences in another way. It indicates the ages by which 1%, 50%, and 99% of the girls in each group have attained the menarche. One girl in a hundred in Colombo has started menstruating by the age of 9 years 11 months, but the corresponding age in the rural girls is 5 months later, in English girls still later by another 5 months, and in Nigeria more than a year after that. One girl in a hundred has still to attain the menarche at the age of 15 years 9 months in Colombo, but it takes a further two and a half years for the rural girls to reach the same state of maturation.

We are not able to offer any convincing explanation of the surprising difference between urban and rural schools in Ceylon. Although the mean age of the menarche in the rural schools accords with that for Nigeria, the figures differ so much in variability that it is not possible to regard even these two sets of data as comparable. It is evident that influences other than the climate must be at work, and our findings suggest that in itself climate may be considerably less important than is often supposed.—We are, etc.,

Oxford. DAGMAR C. WILSON.
IAN SUTHERLAND.

## Iodized Salt

SIR,—The Ministry of Food in its *Food Kitchen Notes* (I.B., April, 1950) states that eventually all salt available to the customer will contain added iodine and that the sale of cut lump salt will be prohibited because it is technically impossible to iodize it. This procedure affords a convenient method of compulsorily administering iodine to those of the population who may need it, but is open to the objection that people who do not require this additional iodine (and they are many), or for whom such iodine may be actually harmful, will not be able to avoid it. The proportion of the population for which it may be inimical is possibly small, but any who may be hypersensitive to iodine should not be compelled to undergo a continual course of enforced iodine medication.

A policy of compulsory dosing with iodine, regardless of whether in any particular case it is necessary or desirable, is objectionable, and ordinary salt should be available for those who wish to avoid such dosing. Moreover, it is unnecessarily wasteful to use iodized salt for many culinary processes, such as the making of freezing mixtures of ice and salt and the preservation of runner beans, where the salt is ultimately washed out of them.

In general, I view with misgiving the tendency to advocate the compulsory "doctoring" of food for the whole population, especially as the dosage thus administered is not governed by the needs of the individual but solely by his predilection for the foodstuff in question. In the event of such ill-advised action as the iodization of all salt, I presume that provision will be made for the supply of common salt (non-iodized) to medical practitioners for the use of patients for whom they consider such salt desirable, and for the preparation by them of sodii chloridum *B.P.* and liquor sodii chloridi physiologicus *B.P.* (normal saline solution), both of which are officially directed to be prepared from common salt and contain no added iodine.—I am, etc.

London, W.14. J. M. HAMILL.

## Intravenous Iron

SIR,—I was interested to read in Dr. A. S. Ramsey's article (May 13, p. 1109) on intravenous iron therapy that in his opinion toxic reactions are avoided if the initial dosage is not greater that 100 mg. of saccharated iron. By and large, I am of the same opinion, but occasional individuals are encountered in whom toxic reactions can occur after such an injection. The following case illustrates this point.

A married woman, aged 35 years, had suffered from anaemia practically all her life. Her count when first seen by me was: R.B.C.s, 4,260,000 per c.mm.; Hb, 42%; C.I., 0.49; M.C.H.C., 26.7%; W.B.C.s, 9,850 per c.mm. There was no obvious cause for her anaemia, and physical examination revealed little of note. She had been given oral preparations of iron of various kinds, but manifested an extreme degree of intolerance to each of them. It was decided, therefore, to give her a course of intravenous iron, and accordingly on March 22, 1950, 100 mg. was given with the usual precautions.

She manifested no toxic symptoms at the time of the injection, but three hours later, when she had returned home, she suddenly sprang a temperature of 103° F. (39.4° C.), accompanied by an intense headache, shivering, and copious vomiting. The severe phase of the attack lasted some six hours and then gradually subsided during the next day. In view of this reaction, on March 25 a reduced dosage of 30 mg. (1.5 ml.) was given, without any untoward effects. And on March 28 a further injection of 60 mg. (3 ml.) was administered. This latter injection was followed by an almost identical reaction to that mentioned above, with the notable difference that it occurred not a few hours after the injection, but two

days later. The patient was put to bed and gradually improved over the next 48 hours, and she was sufficiently well on May 2 to have a further injection, once more reduced to 30 mg. No reaction followed this injection and consequently on May 5 the dosage was increased to 40 mg., which was also taken without any ill-effects.

Subsequent doses of 80 mg. (4 ml.) and 100 mg. (5 ml.) on May 8 and 11 have also been taken perfectly satisfactorily, and her clinical condition is distinctly better. During the 29 days of treatment 27 ml. of saccharated iron has been given, and the haemoglobin has risen during this time from 42% to 69%.

I hasten to point out that this is the only example of intolerance to an initial dosage of 100 mg. which I have encountered in the two dozen cases that I have treated on these lines. Nevertheless, as this form of therapy is likely to become more popular, I think it is important that one should revert to the original technique of Slack and Wilkinson,[1] who recommend an initial dose of 1.5 ml. (30 mg.), followed by a further dose of 60 mg. prior to giving the full dose of 100 mg. (5 ml.). In this way one would be quite sure of detecting the occasional individual who is hypersensitive to this form of therapy.—I am, etc.,

St. Helens, Lancs. F. S. MOONEY.

REFERENCE

1 *Lancet*, 1949, 1, 11.

SIR,—In view of the current interest in the intravenous administration of iron in anaemia I would like to put on record a case recently treated by myself and followed by very severe toxic reaction.

A single woman, aged 36, apprehensive, self-centred, preoccupied with her bodily ailments, had a long history of microcytic hypochromic anaemia. Her blood findings were Hb 52% (Haldane), erythrocytes 4,600,000, C.I. 0.56. Diseases of the kidneys, alimentary tract, chest, reproductive organs, which could possibly contribute to the anaemia, were excluded. I decided to treat her with one massive dose of 1,000 mg. of saccharated oxide of iron, approximately equivalent to the total iron deficiency present in her case. That dose was dissolved in one pint (568 ml.) of the sterile pyrogen-free solution of 5% dextrose and administered in a continuous intravenous drip at the rate of 6–8 drops per minute. This drip was in progress from 9 a.m. to 6 p.m. the same day, during which time no abnormal reactions were observed.

One hour after the discontinuation of the intravenous drip she developed headache, stabbing pain in the back, vomiting, and diarrhoea. She was very pale, her radial pulse became imperceptible, B.P. could not be recorded on the sphygmomanometer, and temperature was subnormal. Immediately the treatment of shock—with warmth, rest, and morphine—was instituted. There was no response to these measures in the next three hours. Her general appearance became worse, her B.P. remained dangerously low, and on auscultation the heart rate was 140. At this stage rapid transfusion of one pint of saline was given, followed by two pints of citrated blood slowly to sustain the rise of B.P. effected by normal saline.

Next morning this patient had vague pains all over her body and felt exhausted and weak. Her B.P. was 140/90 and pulse 84 ; the urine showed a trace of albumin and there were erythrocytes in the sediment. Her further recovery was uneventful ; urine was cleared of pathological components in a few days, and three weeks after her blood findings were Hb 84%, erythrocytes 4,800,000, C.I. 0.87.

In the past twelve months I treated four other cases as above with continuous intravenous infusion of saccharated oxide of iron in doses varying from 500–800 mg. without any abnormal reactions. Nevertheless, the undesirability of treatment with a single massive dose of intravenous iron, as illustrated in the above case, is self-evident. It seems that toxic reactions, characterized by general peripheral circulatory failure, following single large doses of intravenous iron are not uncommon, as appears from my case and the cases quoted by Dr. Ramsey in his article. This general peripheral circulatory failure may be of various degrees of severity and, although usually reversible, in some cases may easily progress to an irreversible phase if it is not treated in time with continuous intravenous infusion of fluids.

I wish to thank Dr. A. R. Grant, medical superintendent of Whittingham Hospital, for permission to publish this case.

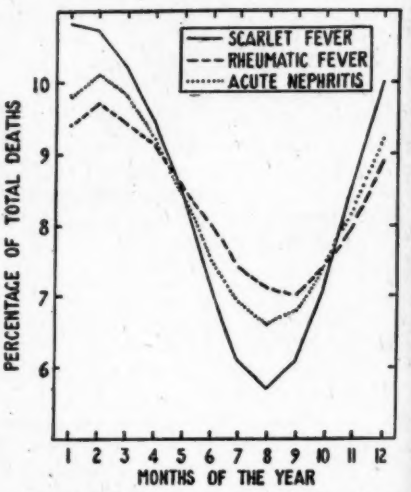
—I am, etc.,

Preston, Lancs. OSKAR J. SLOWIK.

## Scarlet Fever, Rheumatic Fever, and Acute Nephritis

SIR,—Wing Commander T. C. MacDonald's study (April 29, p. 992) emphasizes the closeness of the correspondence in the secular trends of cases of scarlet fever and acute rheumatism. It would be very interesting if similar data could be provided relating to acute nephritis, because there is a considerable amount of evidence that acute nephritis is, like acute rheumatism, an allergic manifestation of invasion by *Streptococcus haemolyticus*. But it has not yet been shown that the secular trend of acute nephritis corresponds with that of scarlet fever, and Wing Commander MacDonald may have access to data which would show if it did.

The effect of seasonal influences upon deaths from these diseases is illustrated in the accompanying figure. The trends are closely parallel. The graph has been constructed from the monthly aggregates of deaths since 1921, when data on this aspect were first made available by the Registrar - General, and relates to deaths occurring from scarlet fever, rheumatic fever, and acute nephritis in England and Wales during the years down to 1947. The curves have been smoothed by the method of three-monthly moving averages, the figures having been first corrected for differences in the length of months. The chief points of note are, (1) the closeness of the affinity between rheumatic fever and acute nephritis, and (2) the relation of both to scarlet fever. The peak of scarlet fever is reached predominantly throughout the years in the month of January, and the peaks of rheumatic fever and acute nephritis in February, and the question arises, Is this an expression of the lag which is part of the field epidemiology of these diseases or simply due to differences in the average duration of the fatal case ?




Seasonal occurrence of deaths from scarlet fever, rheumatic fever, and acute nephritis in England and Wales during the period 1921–47.

I should be glad if any of your readers could supply me with sources of information on the average duration of fatal cases of scarlet fever, rheumatic fever, and acute nephritis in order to help to elucidate this point.—I am, etc.,

Department of Health for Scotland, 20, Renfrew Street, Glasgow, C.2. T. W. BUCHAN, Regional Medical Officer.

## Carcinoma of the Stomach

SIR,—Your leading article on carcinoma of the stomach (April 29, p. 996) is of close interest to general practitioners, because, as you point out, the key to the problem is the earliest diagnosis and the general practitioner is in the most favourable position to ensure the earliest investigation of all suspicious cases. However, as you suggest, it is not always possible under present circumstances for the busy and harassed doctor to refer for fuller examination the numerous cases which complain of indigestion. Nevertheless the problem is not as hopeless as it perhaps appears, for as Mr. H. C. Edwards points out (April 29, p. 973), the tests for occult blood are positive, though not invariably, in most cases of gastric carcinoma. This is in accordance with the findings of Gregersen,[1] Meulengracht and Jensen,[2] and others. It seems, therefore, that a simple and reliable consulting-room test for occult blood could be of great value to the general practitioner in screening cases for fuller investigation.

Tests for occult blood are not now as widely used as they once were, not because they are not reliable, but partly because of the short cut to diagnosis by *x*-ray examination, partly

because of uncertainty about the interpretation of positive findings. In general practice there are obvious objections to a test, such as the benzidine test commonly employed in clinical laboratories, which may give positive results with gum bleeding and after the eating of meat in moderate amounts. With little control over the patient's diet this is sufficient to dissuade practitioners from using the test as a routine procedure.

To overcome this difficulty Gregersen[1] introduced what is now universally known as the Gregersen slide test (G.S.T.). By reducing the sensitivity of the benzidine test to one-third he produced what is now considered to be one of the most reliable tests for everyday clinical use. He discarded the unstable hydrogen peroxide and substituted the more stable barium peroxide in a concentration of 4%. Using a 50% acetic acid solution, the benzidine concentration is kept at 0.5%. The practical application of the test is thus standardized and leaves no room for error. A powder containing 0.025 g. of benzidine and 0.2 g. of barium peroxide is dissolved in 5 ml. of 50% acetic acid. A portion of faeces, the size of a split pea, taken if possible from the interior of the specimen, is smeared on a clean glass slide and a few drops of the reagent are added. In the presence of blood a blue colour, varying in intensity with the amount of blood present, develops in less than a minute. The test takes no more than one or two minutes to perform and is as simple as the consulting-room tests for sugar and albumin in the urine. Because different makes of reagent give varying results, it is advisable always to use the same brand. The benzidine is specifically tested against a freshly prepared 1 in 100,000 solution of blood. The reagents are cheap and retain their efficiency for at least six months. The Gregersen slide test is fully described in Harrison's *Chemical Method in Clinical Medicine*,[2] Hutchison and Hunter's *Clinical Methods*,[4] and in other textbooks of clinical chemistry. It is widely used on the Continent and in America. Ogilvie,[5] after a very thorough investigation, concluded that a blue or blue-green colour, appearing within thirty seconds, is positive proof of the presence of occult blood irrespective of the patient's diet, with the obvious exception of black pudding, liver, bone marrow, and other foods with a high blood-pigment concentration. Meulengracht and Jensen[3] used the Gregersen slide test to investigate 105 cases of alimentary neoplasm in which except in some obvious cases of cancer of the oesophagus and rectum the diagnosis was confirmed by operation or at post-mortem examination. Occult blood was present in 89% of all cases—persistently in 72% and only intermittently in 17%. Only six out of 66 cases of gastric carcinoma showed no occult blood.

I have used the Gregersen slide test in general practice for the past twenty years in the routine examination of my cases, and when in 1941 supplementary rations were granted for peptic ulcer patients my partner and I took the opportunity, using this test for screening purposes, to investigate fully those patients not previously examined who applied for forms R.G.50. Including those investigated over the previous ten years, we collected in our practice 123 cases of gastro-intestinal ulceration in which both *x*-ray and Gregersen slide-test findings were available. There are not included in these figures cases of neoplasm in which, on first examination, the diagnosis was beyond doubt. One hundred and two cases were of peptic ulcer, and 21 of other alimentary conditions. The G.S.T. findings were compared with the *x*-ray and clinical findings, including in some cases confirmation after operation. Both the G.S.T. and *x*-ray findings were positive in 69 (68%) of 102 ulcer cases, and in 18 (86%) of 21 other conditions. The G.S.T. was positive and the *x*-ray findings negative (but clinical observations and subsequent history confirmed the positive diagnosis) in 19 of the 102 ulcer cases and three of the 21 other cases. The G.S.T. was negative, and positive *x*-ray findings confirmed the clinical findings, in 14 of the 102 ulcer cases, but in none of the 21 other cases. Thus there were 22 cases which might have been missed if the G.S.T. had not been used, and 14 cases in which the G.S.T. did not support the diagnosis.

In more than two-thirds of all cases both the G.S.T. and the *x*-ray findings were positive. Of these 87 cases, all but 22 were first diagnosed with the G.S.T. Where the two tests gave differing results the G.S.T. was right rather more often than the *x*-ray findings—22 cases and 14 cases respectively. Of the 19 ulcer cases with initial negative *x*-ray findings, three cases radiographed again after an interval because of a persistently positive G.S.T. gave a positive result, and two cases, one of neoplasm and the other of diverticulitis, both of them with initial negative *x*-ray findings and re-examined for the same reason, subsequently gave positive *x*-ray findings. These five cases are perhaps among the most significant in the series.

As regards ulcers only, both tests agreed in two-thirds of the cases; radiography failed in slightly under one case out of five, and the G.S.T. in slightly less than one out of every seven cases. For the other diagnoses the numbers are too small to give more than a strong indication: 11 cases of neoplasm, five which exhibited diverticulitis radiologically and had a positive G.S.T. (presumably cases of diverticulitis), and one case each of ulcerative colitis, regional ileitis, torsion of the caecum, spastic colon, and pernicious anaemia.

In a leading article[6] some years ago you discussed the necessity for fuller statistics on the incidence of peptic ulcer throughout the country. By the systematic use of the G.S.T. it has been possible in a fairly large industrial practice to achieve a reasonable estimate of the incidence of peptic ulcer. In estimating the value of the G.S.T. (and this of course applies to all the other tests) it is necessary to consider both its advantages and limitations. For the general practitioner it can be a valuable measure in the early diagnosis and treatment of alimentary ulceration. By its use he can sift and control his dyspepsias with more assurance and a better knowledge of the underlying pathology. Often it may enable him to decide more quickly which case requires the more expensive and time-consuming forms of investigation. By taking appropriate measures till all occult blood has disappeared from the faeces it may enable him to evert the more serious complications of haemorrhage and perforation. The minimal amount of blood required to give a positive result varies from one person to another, so a negative finding must not be considered conclusive and should always be judged in relation to the clinical picture. A positive result is always significant, and, provided precautions have been taken to exclude extraneous sources of blood, an attempt must always be made to trace the cause of the bleeding.

As you suggest, a busy doctor may hesitate to refer a patient for fuller investigation before trying the effect of diet and alkalis. By the wider use of the G.S.T. a more scientific control of alimentary ulceration becomes possible, and a situation created where Mr. Edwards's hope for an improved attitude to gastric carcinoma may become a reality. The general practitioner, too, would be greatly relieved of one of his major anxieties—the thought of missing the early and curable stages of malignant disease.—I am, etc.,

Edinburgh. S. LIPETZ.

REFERENCES

1 *Ugeskr. Laeg.*, 1916, **78**, 697, 752, 1197, and 1260.
2 *J. Amer. med. Ass.*, 1929, **92**, 697.
3 *Chemical Methods in Clinical Medicine*, 1947, London.
4 *Clinical Methods*, 1949, London.
5 *British Medical Journal*, 1927, **1**, 755.
6 Ibid., 1944, **2**, 665.

## Spinal Analgesia for Caesarean Section

SIR,—Women undergoing caesarean section under spinal analgesia who cannot breathe comfortably until after the baby has been delivered—Professor R. R. Macintosh (May 6, p. 1076) describes this as not uncommon—have possibly been paralysed to too high a level. Anaesthesia to the 10th thoracic segment is sufficient for a caesarean section, and it seems likely that this limitation is really the most important safeguard. A pregnant woman does suffer many changes—"subtle biochemical" and other—including the development of a more labile blood pressure.—I am, etc.,

London, W.C.1. SHILA G. RANSOM.

SIR,—I am reminded by the correspondence based on the article by Dr. A. H. C. Walker and myself (April 22, p. 938) of an aphorism attributed to Nietzsche: "The shortest distance between the mountains is to step from peak to peak, but for that thou need'st long legs." How often has a doctor working in the Tropics sighed, "If only those back home would

appreciate the conditions under which we work." Much of the comment on our paper was, in the circumstances, a counsel of perfection. Indeed, we were fully aware of the contraindications to the use of spinal analgesia (and especially "stovaine") in both of our cases, but the alternatives were such that we considered the risks worth taking. It is well to remember that Dr. Walker had to build up a univerity department in Nigeria from the beginning, that drugs and equipment often took months to arrive in Ibadan, and that we were often operating single handed (one of us was on leave for one or other of the two operations reviewed). We were without oxygen, and stovaine (Barker's solution) was the only spinal analgesic available. Is it, therefore, a necessary or worthy criticism for Mr. W. G. Mills (May 13, p. 1137) to presuppose that our technique must also have been faulty? Dr. J. A. Lee (p. 1138) writes that "spinal analgesia should have no place in the practice of a surgeon who claims he is obliged by circumstances to manage alone," but I believe that Dr. F. L. Robertshaw (p. 1137) is more realistic when he says, "There remain occasions when spinal analgesia, properly used, may be safer for both mother and baby than general anaesthesia by untrained anaesthetists."

Our paper was written in the interests of spinal analgesia, not in an attempt to condemn its use in caesarean section. It would be misleading if anyone used our experience to further the cause against spinal analgesia. It was, I believe, this possibility that prompted Professor R. R. Macintosh (May 6, p. 1076) and the other correspondents to emphasize that spinal analgesia is an excellent anaesthetic for caesarean section provided the contraindications are appreciated and the anaesthetist competent.—I am, etc.,

London, E.C.4. STAFFORD MATTHEWS.

## The Medical Bill

SIR,—I was startled to learn from the national press that the new Medical Bill, which proposes among other things a year's "internship" prior to registration, is already in Committee in the Lords, while I have heard little or no protest from the profession. This will, of course, provide the hospitals with a series of residents who will not only be unregistered, and therefore paid less (rumour says back to £120), but who are at the mercy of all and sundry, for they will be dependent on their post to attain registration. Moreover, the medical profession will be the only body in the country who will be subject to direction of labour, for that is an inevitable corollary of the proposals.

The Royal Colleges, universities, and other bodies are also being insulted by being told that those to whom they issue a licence to practise medicine are, in fact, unfit to do so. I feel it to be a serious matter that this threat to professional freedom has gone thus far unchallenged. May I add I have no axe to grind? I am a year qualified and still doing house jobs, but I know what my feelings would be were I, as a student approaching qualification, faced with this piece of legislation.—I am, etc.,

Ashford, Middlesex. J. KEITH CARTER.

SIR,—Under the Medical Bill now before Parliament full registration is in future to be withheld from a medical student until he (or she) has done, subsequently to qualification, a period which cannot be less, but may be more, than 12 months' certified *resident* medical service in an approved hospital or institution. This change is to take effect upon a day to be appointed by the Privy Council.

There is in the Bill nothing to limit its operation to new entrants to the medical schools; and, unless something is done about it at once, many men and women who entered the schools on the basis of the old conditions of registration and have already done several years of training will on the appointed day find themselves bound willynilly by the new restriction. This would be retrospective legislation with a vengeance—retrospective without even the semblance of that prior warning with which Sir Stafford Cripps excused himself in an analogous case recently.

Many of those affected—especially the ex-Service men—are getting on in years. Many are married, often with children. For some at least of these the new requirement may well prove a grievous burden, involving further separation from home, the expense and inconvenience of a double establishment, and so on.

I am in no way challenging the principle of more experience before full registration. But however desirable that principle may be *per se*, it must surely be wrong to apply it, without notice and compulsorily, to the detriment of those who signed on, and have already done much of their training, under the old conditions.—I am, etc.,

Guildford. W. B. MANLEY.

## Administration of P.A.S.

SIR,—I have had my first experience recently of giving a patient, a man of 42, a four weeks' domiciliary course of streptomycin daily together with 5 g. of P.A.S. dissolved in 1 oz. (28 ml.) of water and taken four times a day. Incessant vomiting or retching even with only 2 dr. (7 ml.) of the solution put a stop to the P.A.S. Before the end of the four weeks' course of streptomycin a severe haemoptysis intervened, and we have since felt afraid again of trying to give him P.A.S. I understand now that 2½-g. doses are considered sufficient, but he could not take even one-quarter of that.

The patient's condition has been very promising, and I was very loath to give up anything which seemed to do him good. So I sought the aid of Mr. Longhurst, a chemist in this town. He got a number of hard gelatin capsules, each holding just 1 g. of P.A.S., and enteric coated or keratinized them by soaking them in formalin for 20 minutes. We found that after soaking them for 12 hours in HCl and pepsin of the strength of gastric juice the capsules remained hard, but that after soaking in weak bicarbonate of soda and liq. pancreatini for eight hours the capsules were much softened but intact. We then repeated the experiment, reducing the formalin soaking to 15, 10, and finally 5 minutes, after which time the capsule resisted soaking in artificial gastric juice for eight hours, but disintegrated in two hours in the alkaline solution.

My patient has for 18 days taken five of the capsules full of P.A.S. three times a day without any nausea or even diarrhoea, and a search of his stools has produced no intact capsules. Should not this, therefore, be the method of choice of administering P.A.S. to those intolerant to it?—I am, etc.,

Bracknell, Berks. R. H. P. HICK.

## The G.P. at the Crossroads

SIR,—Having for years advocated in print the cause of the general practitioner, I am much concerned by the sad but temperate letter of Dr. E. Anthony (May 6, p. 1077). The crux of the matter is the need of a good general-practitioner service, and, according to Dr. Anthony, under present conditions of the National Health Service this is impossible. Smaller panels with an increased capitation fee would indeed help, if sufficient general practitioners are to be found to take on the people the reduction of the large panels would then leave doctorless.

To leave panels at their present size and to increase the capitation fee would simply increase the incomes of doctors now doing, perforce, their work hurriedly and, in consequence, unsatisfactorily. Good general-practitioner work would save the country immense sums. The general practitioner is without doubt the backbone of the medical profession. The backbone among the lower animals is often prolonged into a tail. There is also a tail to the medical backbone. As I maintained in my presidential address to the West London Medico-Chirurgical Society, a tail is unavoidable, but we must do our best to see that it is wagged properly. We must plan how to put our house in order, and, having arrived at a satisfactory plan, strive to have it implemented and have the service properly remunerated.

As a general practitioner now retired from being for 35 years a part-time hospital pathologist, and having a regrettably small N.H.S. panel and little else, I hesitate to criticize my fellow practitioners, but I do regret the tendency of the general practitioner, whether forced by circumstances or not I do not know, to refer so many of the patients to hospitals and clinics for diagnosis and treatment. One of my surgical colleagues has told me that some of the cases referred to him are of the most trivial nature, such as any general practitioner could deal with.

Pressure should be exerted to hasten the development of health centres, providing for the general practitioner pathological laboratory, *x*-ray means of diagnosis, and the more ordinary forms of physiotherapy. The Ministry of Health has informed me that it must first provide these for the hospital. Will nobody understand that careful investigation while the patient is under the care of the general practitioner, the first person to be consulted, would prevent the subsequent ill-health of many patients and save many lives? And were the general practitioner properly trained for his work he could, by careful observation and without overmuch help from laboratory or radiology, contribute much of advantage to the advance of medicine. In a memorandum to the conference of delegates from the universities and Royal Colleges, met to consider alterations in the medical curriculum, I advocated a special course of training for the general practitioner, whose work differed so much from that of the consultant and specialist. Although I was thanked in a letter from the late Lord Dawson of Penn, the chairman, I do not think my contention received much support. To-day I have turned to a book published by the Edinburgh Pathological Club, giving the contributions of many teachers and other doctors to an inquiry into the medical curriculum (1917–1918), which had been sent to me to review. The first essay is by Sir James Mackenzie, the whole of which is worth study. From this I quote:

"Consider for a moment who is the individual in medicine who has the opportunity for a broad outlook and whose life work gives him the opportunity of seeing all parts of medical science in its true perspective. It is the general practitioner. He sees the conditions which predispose to disease; he sees its inception and the course it pursues, passing from the signs for medical treatment to the time when it calls for surgical interference. He sees the after-effects of the operation after the surgeon has claimed it as a success. If he is stimulated to inquire into the symptoms of disease, he is brought in contact with every special department, and has the opportunity for estimating them at their true value."

Two more passages in this address are worth noting. Sir James wrote:

"It is recognized by every general practitioner who gives the matter consideration that his education was woefully inefficient"; and he concludes, "I have shown that there are fields of research unexplored which hamper progress, which only the general practitioner can work."

The transmission of knowledge is not along a one-way street from the schools to the general practitioner. It may be the most frequent direction in which knowledge passes, but it can proceed in the opposite direction. Robert Koch began his bacteriological researches while a district medical officer in East Prussia, and Sir James Mackenzie did most of his important work on heart diseases while a general practitioner in Burnley. How true is Sir Robert Hutchison's statement that no one is too good to be a general practitioner, and, if the latter is sometimes overawed by remarkable and interesting cases so ably demonstrated at the hospitals by most helpful consultants, let him bear in mind the saying of another learned physician, the late Sir James Goodheart, "Common things most commonly occur."—I am, etc.,

London, W.8. HAROLD H. SANGUINETTI.

SIR,—Dr. E. Anthony's letter (May 6, p. 1077) must express the views of thousands of G.P.s. The art of medicine has disappeared, we have become shopkeepers, "bureaux of information," commissioners of oaths, everything under the sun but true "healers." My one great worry is to get all the work done in 24 hours. When day is done and one reflects on one's activities of the previous 24 hours, is it not soul-destroying and demoralizing to observe how little useful and satisfactory work has been done?

In present conditions the patient has gained nothing and lost much. After waiting two or three hours he spends two or three minutes with his doctor, who often has to diagnose "at sight," for how is it possible to examine carefully (which should be the case) some 60 or 70 patients at one surgery sitting? If the inhabitants of Mars are able to see what goes on here they must wonder what an extraordinary specimen man is. That he cannot exist without consuming gallons of medicine and a thousand and one pills would appear to indicate his imminent extinction. Yet this is not too fantastic.

The mentality of the present-day patient has been influenced by disease-consciousness. Disease is abnormal and unlikely, but he thinks that he is ill until reassured to the contrary. Only about 5% of all visits and consultations are justifiable. This is, I think, the greatest problem. Let us start first by educating the public to think "healthily" through periodicals, films, radio, etc. Let us inculcate into them the notion that disease is not the usual characteristic of life, but the reverse, that simple common-sense measures will be sufficient to overcome trivial ailments, that elementary hygiene will safeguard them against infection. This campaign would certainly tend to eradicate the ever-increasing number of psychoneurotics and *malades imaginaires* which constitute the bulk of our patients.—I am, etc.,

Barkingside, Essex. J. F. PAYAN.

SIR,—I should like to correct one mistake in the otherwise excellent letter by Dr. E. Anthony (May 6, p. 1077). He states: "The doctor now feels that he is chasing his practice downhill all the time with no hope at present of ever catching up." May I point out that we have no practices: these were taken from us on July 5, 1948. Has Dr. Anthony so soon forgotten the heavy fine and imprisonment to which he is liable if he tries to sell what he thinks is his practice? This may be the missing link for which he seems to be so fervently seeking.—I am, etc.,

Leigh-on-Sea, Essex. THOMAS REES.

## Morphine in Acute Chest Infections

SIR,—"T. G." is to be congratulated in giving publicity to the dangers of giving morphine to patients with a history of asthma (April 22, p. 958). Morphine causes progressive slowing of respiration by depressing the respiratory centre and rendering it less sensitive to afferent stimuli through the vagus. But as it does not equally decrease the responsiveness of the centre to carbon dioxide stimuli, respiration becomes also progressively deeper. The increased depth, however, does not compensate for the slowing, and symptoms of anoxaemia and asphyxia ensue.

The danger of morphine in asthmatics is marked. Administration of ordinary doses appears to quieten the patient, but as the paroxysm passes off large amounts of mucus are secreted, and, morphine having depressed the respiratory centre and reduced the cough reflex, asphyxia supervenes and the unfortunate patient may die in his sleep. In status asthmaticus final resort may have to be made to morphine, but it should only be administered in small doses of 1/12 gr. (5.4 mg.). Provided there are no marked changes on the respiratory centre this dose may, if necessary, be repeated in half an hour.—I am, etc.,

Worthing. E. W. THOMPSON EVANS.

## Training of Medical Artists

SIR,—I was most interested to read Professor Geoffrey Jefferson's letter (March 25, p. 728) on the training of medical artists, in which he replies to an earlier letter of mine. But I am sorry that in my letter I gave the impression that the committee of the Medical Artists' Association of Great Britain intended to take steps to suppress the apprenticing of trainees to medical artists holding hospital and university appointments and compel all trainees to go to a school of medical art.

It has never been the intention of the committee of this association to take any steps in this direction. It was my intention to suggest that there would be advantages in medical artists being trained at one centre. If half a dozen pupils were being catered for it would be possible to arrange a more complete course for them—including, for example, a sound grounding in anatomy—than is possible in the case of a single apprentice pupil. While the risk of medical illustration becoming stylized is increased, the risk of some pupils training under inferior instructors is reduced.

After reading Professor Jefferson's letter I agree with him that the present system is probably the more satisfactory. In any case, what is desirable and what is practicable are often

two quite different things, and on economic grounds alone it would not be possible for all students of medical art to receive their training at one centre. I should like to add that it has never been suggested that the possession of the Edinburgh certificate of medical illustration should be considered as a qualification for admission to membership of this association. We have our own board of examiners, consisting of two medical artists and also a distinguished anatomist and an equally eminent surgeon.

If anyone felt that the splendid work being done at various hospitals and universities in training future medical artists was being disparaged, then I would like to assure him that this was not the case.—I am, etc.,

DAVID TOMPSETT,
Chairman of Medical Artists' Association of Great Britain.

London, W.C.2.

## Mass Vaccination

SIR,—Recently two cases of clinical smallpox and one suspect occurred in this district. A mass vaccination campaign was launched, and over 30,000 people were vaccinated in a week.

The question is whether mass vaccination is justifiable in smallpox outbreaks in this country. It seems to me that mass vaccination is an anachronism in a society with a highly organized health service and that the main lines of attack are: (1) selective vaccination of contacts and medical and nursing personnel at risk; (2) isolation of all patients with undiagnosed febrile illnesses; and (3) quarantining of contacts. Only where the contacts get out of hand should resort to mass vaccination be necessary.

I am purposely omitting reference to the trouble, expense, and panic associated with mass vaccination campaigns, the dangers of vaccination, and the fact that none of the cases in this area was subsequently confirmed, because all these items are secondary to the main question—whether mass vaccination is necessary for the control of outbreaks of smallpox in this country.—I am, etc.,

Halifax. A. W. FOWLER.

## The Maternity Service

SIR,—The letter on this subject by Dr. J. S. Laurie (*Supplement*, April 22, p. 177) voices a legitimate amusement on the part of the medical profession about the Government and the R.C.O.G. claiming credit for the reduction in recent years of maternal mortality. But it also affords a streak of amusement to those who initiated the birth-control clinic service, and who know that the now widespread use of birth control by women who are in a state of ill-health and unfit to bear children also plays a very important part in the reduction of maternal mortality.—I am, etc.,

London, W.1.

MARIE C. STOPES,
President of the Mothers' Clinics for Constructive Birth Control.

## British Spas and Health Resorts

SIR,—A group of medical men interested in physical medicine, and particularly in the therapeutical powers of the British health resorts and spas, have held some preliminary meetings for the purpose of discussing the methods of study and development of these resorts. It was decided not to revive the pre-war British Health Resorts Association but to create a new organism, a new association, including medical and non-medical men interested in this question. As hon. secretary of these meetings I was entrusted with the task of ascertaining the views on this subject of the British medical profession, and I should be grateful to receive any comments on this plan for the development of our spas and health resorts.

Great Britain possesses some of the finest spas and health resorts in the world, and it is, in fact, in this country that modern climatotherapy originated. The renewal of interest in the method of physical medicine, the difficulties of travel abroad, and the desire to bring into this country many overseas visitors are sufficient factors to stimulate us to more definite action for the development of these outstanding physical therapeutical agents.—I am, etc.,

7, Wimpole Street, London, W.1. A. P. CAWADIAS.

## Brachial Neuralgia

SIR,—I read Dr. W. M. Philip's article (April 29, p. 986) with interest and some surprise. In the paragraph on differential diagnosis the author surprisingly omits a, in my experience, very frequent and important group of painful arm conditions which are purely muscular in origin and due to an idiopathic myalgia.[1] Dr. Philip's paper refers to 66 ambulatory patients with "pain radiating down the arm," of which 24 cases, belonging to a miscellaneous group, defied classification. But in 42 cases "it has seemed probable that the symptoms were the result of compression of one or more cervical roots."

The diagnosis was made primarily "on clinical grounds" and based on: (1) referred pain of dermatome-like distribution; (2) tenderness and pain in the muscles supplied by the same spinal nerve (root); and (3) *x*-ray changes corresponding to the root involved. I feel bound to say that the clinical and other evidence is not conclusive nor suggestive, for the following reasons. It has been known for many years that referred pain of dermatome-like delineation is very characteristic of muscular diseases. Further, the modern diagnosis of myalgia is based on objective criteria and characterized by the triad referred pain, loss of power (weakness) in a muscle or muscle group, and paraesthesia. In addition the procaine injection of the specific "myalgic spots" may serve as a diagnostic test to prove conclusively whether or not a myalgia is responsible for the symptoms and signs in a given case. By contrast the diagnosis of "root irritation" is based on theoretical considerations which cannot be proved objectively.

As far as *x*-ray findings are concerned, the author himself stresses "one rather striking feature"—that gross osteophytic protrusion into the intervertebral foramina can occur without the production of symptoms. Why then, one may ask, is the narrowing of the intervertebral foramen conclusive evidence for "root irritation"? No evidence has been adduced to show that variations in the width of the different intervertebral foramina are not found in normal persons. On theoretical grounds it would seem reasonable to expect such variations, since the thickness of the spinal nerves is not a constant. According to Dr. Philip the earliest radiographic sign is the loss of the normal curve. I am, however, of the definite opinion that this symptom is caused by an unequal tonus (degree of contraction) of the cervical muscles attached to both sides of the vertebrae: under normal conditions the antagonistic pull of the right and left cervical muscles—especially the trapezii—keeps the vertebrae in a straight balance.

Lastly Dr. Philip seems to support the diagnosis of brachial neuralgia by comparing it with the syndrome of sciatica, which "is well recognized as due to a prolapsed intervertebral disk resulting in irritation of a single root." For years I have been emphasizing that the majority of cases of sciatica are muscular in origin—"muscular sciatica"—caused by a polymyalgia of hip muscles (quadratus lumborum, glutei, tensor fasciae latae), and can be cured by procaine injection of the appropriate myalgic spots without ever resorting to the ordeal of a laminectomy.—I am, etc.,

London, N.W.11. M. G. GOOD.

REFERENCE

[1]Good, M. G., *Lancet*, 1940, **2**, 326.

## Maternity and the N.H.S.

SIR,—In his endeavour at over-simplification Dr. C. Iliffe (May 6, p. 1080) manifests himself as a victim of the age which lauds institutional treatment and can view domiciliary practice only as second best. Happily he would seem to sense the foolishness of his arguments based upon false premises, as evidenced by his fondness for the word "surely."

I regard childbirth away from the home as an unfortunate anticlimax for the parents and cannot conceive a more joyous home than one in which lie an infant and its mother. The significance of this with regard to the future stability and well-being of the family is not to be lightly dismissed, nor must one ignore the unrest of the mother in hospital, so completely divorced from her husband and possibly her family.

It is not perhaps properly realized that a general practitioner has frequently to guard his patients against too great a readiness

to seek relief of their ills in hospital. Among the more academic physicians a simple malady—curable or otherwise—can easily become a great test of physical and mental endurance, and it is a commonplace that the heroism of some surgeons exceeds that of their patients.

That there are hazards attendant upon hospital treatment much less likely to be met with in the home must be accepted, and the wise surgeon is ever on guard against the fallibility of his team. Injection of the wrong fluid, dangers associated with the more complex anaesthetic machines, and cross-infection of mother and/or child spring readily to mind. The inexperience of the junior nurse on duty and over-confidence of the absent sister were recently the cause of two women known to me in different parts of the country—one a primipara—giving birth to their children completely unattended while lying in their ordinary main-ward beds. Both of these patients had been booked and admitted, despite the bed shortage, because it had been judged safer to do so.

The surgeon himself cannot remain free of criticism, either of omission or commission according to the bent of his enthusiasm. It is a truism that no one is better for an operation if it can reasonably be done without, but woe betide the student who has not acquainted himself with his external examiner's views regarding the indications for or against caesarean section.

In common with others, Dr. Iliffe's ideal would be to have everyone cared for by a specialist—an unfortunate name for a doctor which I would like to think was only used by a layman to indicate perhaps some measure of academic brilliance. As a practitioner I endeavour to refer my patients to consultants whose special knowledge and success are linked with wisdom based in part upon past mistakes, which are aired from time to time for teaching purposes. In my opinion domiciliary midwifery is the ideal, and, lacking special indications, hospital management is only second best.—I am, etc.,

Malvern, Worcs. G. A. FLANN.

SIR,—I should like to respond, somewhat inadequately I fear, to the letter of Dr. C. Iliffe (May 6, p. 1080). It is regrettable that such an attitude of mind is patent in a member of our profession. Such views if expressed by a lay medical administrator would not be in the least surprising, but to come from one of our brethren strikes me as being peculiarly tragic. He writes: "Any maternity case would be safest in the care of the expert and in a place where every facility was available to deal with any complication." Now nobody can of course deny this, but does your correspondent seriously suggest that every potential normal confinement should be under the immediate control of a specialist obstetrician? I take it that that is what he means by expert. With the latter part of the quotation I would agree most heartily, but consider that the general practitioner should have these facilities at his disposal, and thus widen his scope rather than attempt to restrict it as seems to be the fashion these days.

To take another phrase: "It is surely foolish for general practitioners to insist that in this one realm they are as competent as specialists." Of course it would be foolish, but it just is not true. The general practitioner is not entirely irresponsible and he knows his limitations. Oddly enough, some doctors obtain satisfaction from practising their art to the height of their ability, which is surely an attitude to be encouraged. Midwifery is the basis of general practice and the beginning of the family-doctor–patient relationship, and I think fundamental to cementing that link.

If Dr. Iliffe's proposals are followed to their logical conclusion one might as well argue that because the general practitioner is not an expert in either pure medicine or surgery he should not treat acute tonsillitis or open a simple abscess, and so on. It reminds one of the proverbial walnut and the sledge-hammer. Finally, let it be stated that the general practitioner will not always have an honoured place in medicine if he be forcibly denied responsibility, as your correspondent suggests. This is just one of these empty phrases that one is used to at the present time. If we are to preserve the integrity of British medicine we must resist this awful trend, especially when it comes from within our midst.—I am, etc.,

Camberley, Surrey. J. S. TAYLOR.

## Immunization and Poliomyelitis

SIR,—Some few weeks ago I, like many others, was startled one morning to read the headline in my daily newspaper suggesting that diphtheria immunization caused poliomyelitis. This was certainly the first impression I gained. The general public, even if they read the article through to the end (where the word "pertussis" was mentioned), almost certainly read it as meaning that: (1) injection against diphtheria was the main factor; and (2) the virus was in some way introduced by the immunization.

The reaction amongst mothers was in my experience immediate. Those who are intelligent were naturally anxious but still wished to have their babies immunized against diphtheria after being reassured. The others (and those, alas, with largest families) of lower intelligence have hitherto been able to find no single valid excuse for not accepting immunization against diphtheria. They have immediately clutched at this excuse (as at a straw) and nothing I, or you, Sir, can say will ever make them agree to immunization now. And all this just at a time when immunizations against diphtheria are beginning to drop somewhat. I feel something should be done to curb the enthusiasm of reporters in matters requiring medical knowledge for full understanding. We certainly do not wish to see prophylaxis against diphtheria relegated to the present appalling position of vaccination.

I was very interested in the report (April 29, p. 1004) of the discussion in the Section of Epidemiology and State Medicine of the Royal Society of Medicine at which an account of the work of Professor Burnet and Dr. McCloskey was given. If the incidences of I.P. and inoculations are related at all (and with a well-inoculated child population it is difficult to see how they can avoid being apparently related in some cases), it would appear that those having combined injections suffer highest risk, pertussis alone next, and diphtheria least. Is it not also true that the local (and general) reactions to immunization are also in that order, which points to the possibility that the local state of the musculature is the factor on which the manifestation of paralytic I.P. depends? I believe that it is agreed that fatigue is a vital factor in development of paralysis—i.e., local muscular fatigue—and might this not bear out the possibility of virus development taking place in a locally "receptive" muscle after an inoculation for anything?

Again, the age group in which local reactions occur in inoculations approximates more to that for I.P., and I have never yet seen a severe local reaction (in hundreds of cases) in babies of 9 months. It would appear that there is no danger whatsoever in immunizing a baby (of, say, 9 months) against diphtheria alone. But will the mothers concerned be able to realize this? There will now be a doubt in their minds—particularly as the "facts" were reported not only in our more sensational dailies but also in the more sober ones. The whole subject is worth well ventilating in the medical press, but surely not in the lay press first. And which disease of the two is the lesser evil?—I am, etc.,

Tavistock, Devon. MARY E. BUDDING.

## Rheumatoid Arthritis

SIR,—Dr. Barbara Crawford (May 6, p. 1074) challenges certain figures in the report of the Scientific Advisory Committee of the Empire Rheumatism Council. The figures are, of course, based on patients' statements. One expects patients to know only of arthritis as a whole and not to be aware of any medical subdivisions.

I am quite sure that for every patient who has had institutional treatment for arthritis there must be at least ten, known to their relations, who get on with their pains and aches due to arthritis for which no recorded treatment is given. I would say that there are many more than 2,000,000 cases of arthritis in this country, of which less than 10% receive other than home treatment.—I am, etc.,

London, S.E.3. J. D. DILLON.

SIR,—I would like to draw attention to certain points in the interesting report of the Scientific Advisory Committee of the Empire Rheumatism Council (April 8, p. 799). Attention has

been drawn by Dr. F. Bach (April 22, p. 957) and Dr. A. B. Hegarty (loc. cit.) to that section of the report in which it is stated that the statistics showed that psychological factors played no important part in the aetiology of rheumatoid arthritis. The report, however, states that further investigations are warranted into the familial incidence of the disease. This suggests an inherited susceptibility in a proportion of cases.

The fact that in these statistics there is no evidence of psychological factors being of aetiological importance can only be reconciled with the observations to the contrary of many individual clinicians if we presuppose a predisposition to rheumatoid arthritis either hereditary or acquired in certain individuals. There are parallels to this in other diseases. May I therefore suggest that the Scientific Advisory Committee might consider whether it is feasible to look at the problem from this angle.—I am, etc.,

Winchester. C. B. S. FULLER.

### Tuberculosis and Industrial Injury Benefit

SIR,—Dr. F. Temple Clive (May 13, p. 1143) expresses the concern of many who have the responsibility of recruiting staff into the tuberculosis service. After reading the report at p. 1145 in the same issue of the *Journal* of the findings of the tribunal in this particular case, I am asking you to allow me to put forward some interpretations of risk of infection and subsequent disease.

It appears that the case rests on the difference between a single accidental entry of tubercle bacilli causing disease and the possibility of continued attempts at entry by bacilli constituting a "process" eventually producing disease.

Lurie, of the Phipps Institute, Philadelphia, has proved that one or more virulent bacilli inhaled by a rabbit through a special apparatus produced pulmonary tuberculosis. Such experiments are not likely to be carried out in man. On the other hand, at Lübeck, when in error uninfected children were given a dose of virulent bacilli, infection and disease resulted, but not in all. Some survived. In the case of the survivors all the factors for an accident had not occurred; bacilli were available, but the soil at the time was not receptive.

Virulent bacilli in small or large numbers are only one factor; penetration must be possible, and the soil—the tissues—must be susceptible at that time for infection and subsequent disease process to take place. Surely the synchronization of these factors is chance, an accident. There must be times when tubercle bacilli are inhaled, but not in circumstances to penetrate. Similarly there must arise times when the soil is ready, but bacilli do not alight on that soil at that time.

Inhalation and natural excretion of tubercle bacilli, like other foreign materials, from the respiratory tract of an uninfected individual should not set up any new relationship between his tissues and the bacilli and does not therefore constitute a cumulative process. On the other hand, with the tuberculosis worker inhalation of tubercle bacilli will occur frequently: there will be a high risk of accident—the accident of temporary factors allowing penetration, infection, and disease in the so far uninfected soil being synchronous with the arrival of the tubercle bacillus.—I am, etc.,

Leeds. W. SANTON GILMOUR.

## POINTS FROM LETTERS

### Health and the Soil

Mr. A. WILFRID ADAMS (Bristol) writes: Deteriorating health and exhaustion of soil are two appalling products of our scientific age to which Mr. F. Keith Hayman (April 15, p. 906) directs one's attention forcibly. Science is the handmaid of this decline by its amazing inventions of means to neutralize the harmful effects of indulging human weakness in such matters as snow-white bread and incessant extraction of bumper crops from the soil. . . . The profession tries to find remedies to counteract the resultant evils, but the cost of this process in dealing with dental caries, peptic ulcer, constipation, and a whole train of evils is now confronting the Chancellor of the Exchequer and causing him a headache—more medicine required. Instead, we should tell the Ministers of Health, Food, and Agriculture how to prevent these ills by the care and maintenance of health. . . .

# Obituary

Dr. HENRY HYSLOP THOMSON, who was county medical officer of Health for Hertfordshire, died at his home in Helensburgh on May 2. Dr. Thomson was the eldest son of the late Rev. John Thomson, of Longrow Church, Campbeltown, and was born there. He was educated at the local grammar school, and graduated M.B., C.M. at Glasgow University in 1896, proceeding M.D. two years later. After a short period of hospital and private practice he was appointed medical superintendent of Quarriers' Homes, Bridge of Weir, and of the sanatorium connected with these homes. Although he spent the last twenty years of his working life as a county medical officer of health, it is his work on tuberculosis which will be remembered. From the Bridge of Weir he went to the Liverpool Sanatorium, at Frodsham, Cheshire, and he was also for a short time tuberculosis officer of Newport and East Monmouthshire. Then in 1912, the year in which he took the D.P.H., Thomson was appointed county tuberculosis officer for Hertfordshire. This was one of the first posts of its kind, following the passing of the National Insurance Act, and the appointment was separate from that of the county medical officer. At first the referring of patients for diagnosis and treatment to an "official" was not readily acceptable to many general practitioners. It was only by his marked clinical ability together with his tact and popularity that Thomson was able to meet this rather difficult situation. On the retirement of Sir Francis Fremantle in 1920 he was appointed county medical officer and school medical officer, in addition to the duties as county tuberculosis officer. Although very much of his time from then onwards was spent in other work, nothing pleased him more than to attend a tuberculosis clinic during the temporary absence of one of the tuberculosis officers. He was an indefatigable worker and in addition to writing many articles on tuberculosis was also author of *Tuberculosis; its Prevention and Home Treatment*, and *Tuberculosis and National Health*. He was also one of the joint editors of *Principles and Practice of Preventive Medicine*.

Thomson reached retiring age in 1940 and since then had lived in Helensburgh, Scotland. He had been a member of the B.M.A. for many years, and was president of the Cambridgeshire and Huntingdonshire Branch in 1926–7, and chairman of the East Herts Division in 1933–4. He leaves a widow and two daughters.

Dr. BENJAMIN ALFRED PETERS, who died on May 8, retired from the position of medical superintendent of Ham Green Hospital, Bristol, in 1948. He was reader in infectious diseases at Bristol University. He graduated at Cambridge in 1908, took the Cambridge D.P.H. in 1910, and proceeded M.D. in 1913. He went to Ham Green Hospital in 1910, and his service with the hospital was broken only by the first world war, when he was a captain in the R.A.M.C. and bacteriologist to the 14th General Hospital.

R. H. P. writes: During his stay at Ham Green Dr. Peters played a great part in the expansion and development of the hospital. When he went there in 1910 it had only 200 beds for infectious diseases; 136 sanatorium beds had been added by 1919, and the accommodation has since steadily increased. During the last war Charterhouse Hospital, with over 100 beds for fever and tuberculous cases, also came under his care. His chief interests were fevers and biochemical research, and his work on diphtheria antitoxin and other antibacterial sera was well known. His research into the cause and treatment of gastro-enteritis in children was of great value, and the mortality from this disease was always outstandingly low in his hospital. He was the author of many papers to the medical journals. Although his retirement was brief he continued to interest himself in research in the laboratory of the hospital. The University of Bristol recognized his work in teaching undergraduates and graduates and awarded him the Markham Skerritt prize. He leaves a widow and one daughter.

# Medical Notes in Parliament

## MEDICAL BILL

The report stage of the Medical Bill was taken in the House of Lords on May 16. Lord SHEPHERD moved to add to subsection (4) of Clause 14, dealing with the disciplinary committee, a provision that

"at any such hearing at least one of the members who are neither registered practitioners nor the holders of qualifying diplomas shall be eligible to attend."

Lord Shepherd said that during the Committee Stage Lord Nathan had proposed an amendment that there should be at least one lay member of the Disciplinary Committee of the Medical Council on any committee of nine or on any quorum of five when cases were under consideration. By agreement the Government now brought forward this amendment to take the place of that previously proposed by Lord Nathan.

Lord LLEWELLIN said that this amendment met the point on which all were agreed, and he supported it. The House then agreed to the amendment.

On Clause 21 Lord SHEPHERD moved to insert in subsection (1) after the words "the Council may appoint persons not being members of the Council to visit," "subject to any directions which the Privy Council may deem it expedient to give and to compliance with any conditions specified in such directions." He said that since the Committee Stage the Government had reached agreement about appointment of visitors by the General Medical Council to schools and examinations. That agreement was embodied in the amendment under which the initiative for the dispatch of visitors to schools and examinations would be taken by the General Medical Council. When that Council reached a decision, it would communicate with the authorities concerned and discuss the conditions under which a visit would be made. There would be talks and, he hoped, agreement. If agreement was reached, the visitors would proceed and there need not be a recourse to the Privy Council. Satisfactory discussions had already taken place between the General Medical Council and the University of London. It was proposed that the persons who were to make the visits should by agreement be appointed to act both as external inspectors on behalf of the University and as visitors for the General Medical Council, thus avoiding two separate inspections. Should no agreement be reached between the two bodies some trouble would arise unless provision was made to meet it; under the amendment the University or the school on one side, or the General Medical Council on the other, could, if they so wished, approach the Privy Council asking that directions should be given on the procedure that would be followed. The Government trusted that as a result of this amendment and of the spirit which animated the parties concerned an early working arrangement would be achieved.

The amendment was accepted without debate, and the Report Stage concluded.

## MIDWIVES BILL

The House of Commons on May 15 went into committee on the Midwives (Amendment) Bill. On Clause 1 Mr. BLENKINSOP moved to insert a new subsection:

(2) An order under the foregoing subsection may provide for any incidental or supplementary matters for which it appears to the Minister requisite or expedient for the purposes of the order to provide and in particular, but without prejudice to the generality of this subsection, may (so far as provision in that behalf appears to the Minister to be requisite or expedient for the purpose of giving full effect to the order) provide that the power of the Central Midwives Board under section three of the Midwives Act, 1902, to frame rules with respect to such matters as may be specified in the order.

This amendment was to ensure that the original wording of the clause should not be needlessly restricted. The Minister, after discussion with the Central Midwives Board and other interested bodies, might desire to put before the House an order requiring steps to be taken in connexion with elections to be carried out to the Central Midwives Board. The department had been advised that if the Minister wished to do so he probably could not under the wording of the Bill as it stood. Further, if it were desired at any time to secure elections to the Central Midwives Board, it would be necessary for the Board to be empowered to make rules to carry out the order. For these reasons the Ministry felt it necessary to have the rather wider powers which were covered by this amendment.

The Chairman, Major MILNER, suggested it would be convenient to discuss at the same time amendments dealing with Scotland. After some discussion the House agreed to the amendment proposed by Mr. Blenkinsop, and accepted further consequential amendments relating to Scotland. Clause 1 as amended was then ordered to stand part of the Bill, as were Clauses 2, 3, 4, and 5.

### Midwives' Uniforms

Mr. WILLIAM ROSS then moved to delete words inserted in Clause 6 by the House of Lords, which gave a right to the midwife to wear the national uniform if she wished. Mr. Ross said it would be better to leave the Midwives Board to draw up the rules and to provide what flexibility it thought fit. In conferring an absolute right upon a midwife to wear the national uniform difficulties would be created with midwives in municipal services where each local authority had been accustomed to supply a uniform of its own design and colour to all outdoor nurses, including midwives.

Dr. CHARLES HILL hoped that the amendment proposed by Mr. Ross would not be accepted. The main purpose of the clause was to empower the Board to frame rules covering the uniform, and, the Board having designed a uniform, it was reasonable to add that midwives should have the right to wear that uniform should they so desire. He did not agree that if the work of the Board in designing the uniform found expression in the wearing of the uniform by midwives the power of the Board would be limited in any way. He appreciated the argument put forward by Mr. Ross that if a right were given to a midwife to wear the nationally approved uniform some conflict might occur between local uniforms and the national uniforms. On balance he thought it right that when everyone desired that the status of the midwife should rise and be recognized there should be a national uniform which midwives everywhere could wear. Such a nationally adopted and worn uniform was to be preferred to the competitive efforts of local authorities. He believed that midwives generally would adopt the uniform, and he hoped the Minister would resist the amendment.

Mr. SOMERVILLE HASTINGS also hoped that the Minister would not accept the amendment. It was reasonable that midwives should be able to wear the national uniform when they so desired. Midwives should be recognized by everyone wherever they went.

Miss HERBISON, speaking for the Scottish Office, said the Government felt the words proposed to be left out were open to objection. They purported to give to midwives, including those in the service of the Crown and the hospital boards, a right to wear the midwives' uniform irrespective of conditions of service entailing the wearing of some other uniform. The Department of Health for Scotland and the Ministry of Health for England and Wales felt this was unjustifiable interference in a matter better left to arrangement between employer and employees. There seemed doubt in the minds of Members whether the words inserted in the House of Lords really secured to midwives the right claimed for them. Before the Bill reached the Statute Book the Government would like it to be clear that the words secured that right. Even if they did secure it, the words which were now proposed to be left out would be objectionable as leaving in considerable doubt the precise extent of the rights of midwives. On all counts, therefore, the Government was willing to accept Mr. Ross's amendment. The words originally in the Bill had given the same rank to midwives as the Nursing Act had given to all other nurses in Great Britain.

Mr. BLENKINSOP said there was difficulty in trying to meet the desire that there should be a national uniform. Was it to be worn by those midwives in the armed Forces? Was it intended that the provision should apply to those serving in hospitals as well as to those in local authorities' domiciliary services? He suggested the best thing the House could do was to defer the matter and consider it further before the Report Stage. The Government was anxious that there should be agreement on the point. It desired something which local authorities as well as midwives would be able to accept. Mr. Ross then withdrew his amendment, and the Clause was ordered to stand part of the Bill.

Mr. BLENKINSOP then moved a new Clause which he explained would entitle the Central Midwives Board to vary the fees for examinations, which at present had an upper limit of one guinea in each case. The same power had been provided in an earlier Act in relation to nurses.

The House accepted the Clause and it was added to the Bill. Mr. Blenkinsop then moved another new Clause giving power to local supervising authorities to provide residential accommodation for pupil midwives. He said the Clause restored to the Bill a proposal which for technical reasons had to be withdrawn in the House of Lords. The Clause was added to the Bill.

The House accepted new Clauses on expenses, and another Clause providing that Members of Parliament were not to be remunerated for sitting on either of the Boards. Mr. Blenkinsop said it was desirable that a Member of Parliament should not be prevented from being a member of the Board by the rule which prevented Members from holding an office of profit under the Crown. The Clause provided that a Member of Parliament should not receive from the Board anything beyond his bare expenses for travelling and subsistence. The Committee Stage then concluded.

## DENTAL SERVICES

On May 15 Mr. BAIRD moved the annulment of the National Health Service (General Dental Services) Fees (Amendment) Regulations, 1950. He said all sides of the House would agree that the cost of the general dental services was out of proportion to the cost of the health services as a whole and that there should be some reduction in dentists' remuneration. The cost of the dental services was running as high as the cost of the general medical services, although there were only 9,000 dentists on the register against 19,000 general practitioners. He did not object to a cut, but he thought that Mr. Bevan's method of cutting the remuneration of dentists was wrong. About twelve months ago dentists' remuneration had been cut by some 20%. The Minister now arbitrarily imposed a further cut of 10% in all dentists' remuneration, and the dentist who was slow and a good worker would suffer as much as the dentist who was working as fast as he could to get a large turnover.

If the dental staff of the Ministry of Health were at full strength much better control could be ensured over expenditure. The establishment was of 44 dental officers, but there were only 22. Dentists employed by the Ministry of Health were paid a much smaller income than the Spens Committee had suggested: the Ministry, by expenditure of a few thousand pounds in increasing the salary of the inspectorate, could save millions. He asked if any Government inquiry had been made to see whether this could be done.

Sir HUGH LUCAS-TOOTH said the country spent £48 million on the dental section of the National Health Service last year, which worked out at a gross payment of about £4,800 a dentist, compared with £2,600 a year paid to the doctors within the National Health Service. There was something fundamentally wrong when the average dentist was paid about twice as much as the average doctor. The enormous pressure of work on dentists who were making large incomes was telling on the dentists themselves and on the quality of their work. That was why he thought some limit should be set. If they reduced the fees payable to the dentists to ensure that some of them re-entered the School Dental Service they would find queues grow longer and dentists would tend to go back to private practice.

Mr. BLENKINSOP said both sides of the House had agreed that there ought to be a reduction in the cost of the dental services and that the figures now earned by dentists were higher on the average than the country could reasonably be expected to pay. Even assuming that the proportion of expenses was at the rate of 52%, that left dentists an average income of £2,250 against the figure of approximately £1,800 a year which the Spens report had recommended. There was no doubt the figures now being paid must be further reviewed. It was clear from the Penman Report that 33 chair-side hours were not being worked. There was no question of an arbitrary cut. There had been discussions with the dentists on this matter, but it could not be left for an indefinite time while alternative proposals were being worked out. A letter to the British Dental Association had made it clear that the Government did not put forward this scheme as a final proposal and was most anxious to consider alternative ones. The door was still open for negotiations and discussions should the dentists come forward with further proposals. The Government was not satisfied that the proportion of 52% for dentists' expenses was accurate to-day. A review was being carried out into the actual amount of these expenses. He asked that the Prayer moved by Mr. Baird should be nullified on the ground that the cut which the Government had imposed was an interim one and that it was willing at all times to consider alternative proposals.

Dr. CHARLES HILL said the House had discussed how an economy could best be made, bearing in mind that the mode of effecting it could have an effect on the working of the service. There were too few dentists to provide a comprehensive service. The dental profession had to work longer and quicker than was reasonable, with a lowering in the quality of the service in some instances. Did the Government want an attempt to be made to provide the promised comprehensive service for the whole of the community? If not, and if the Government sought to maintain good quality of dental work, a decision had to be made on which group was not to have the service which had been promised. There had been no attempt to answer that question. It might not be impossible to exempt remuneration received from local health authorities for school dental work, or work done for priority groups like schoolchildren and nursing and expectant mothers, from the maximum limitation scheme. The Government would sooner or later have to face the fact that if there were too few dentists to provide this service then the Government must itself decide who had to come first. He hoped the Government would not continue to put off the main issue.

Dr. H. B. MORGAN asked whether Dr. Hill was moving towards a proposal that priority work should be paid at a higher rate than ordinary treatment for ordinary people.

Dr. HILL said that if there were to be rates of remuneration which differed above and below a given line it would be reasonable to exempt work done for defined priority classes from the operation of that maximum.

Mr. BAIRD, replying to the debate, said he thought the problem would not be solved until the country had a fully salaried dental profession. He spoke of the shortage of dentists.

Dr. HILL remarked that, before the war, in the dental profession alone among all professions there had been fewer entrants than people who left the profession.

Mr. BAIRD said the reason for the shortage was that to-day there was a bigger demand for dental treatment. He believed that if the Ministry made a gesture the dental profession would welcome the opportunity of entering again into negotiations. The deadlock would not be broken simply by imposing arbitrary cuts. He then withdrew his motion.

# The Services

Colonel (temporary) (Local Brigadier) C. M. Marsden and Captains M. H. F. Coigley and A. K. Thomas, R.A.M.C., have been mentioned in recognition of gallant and distinguished services in Malaya during the period July 1, 1949, to December 31, 1949.

# Medico-Legal

## NO INDECENT ADVERTISEMENT

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

The police of Stalybridge recently prosecuted Mr. William P. Quinn, a shopkeeper in the High Street there, for unlawfully exhibiting indecent printed matter in his shop window.[1] They proceeded under the Indecent Advertisements Act, 1889, which prohibits the affixing of indecent advertisements to premises, and sought to show that the title of a book displayed in the window, *Venereal Disease: Its Prevention and Conquest*, was an advertisement, and that to exhibit such an advertisement in the window was equivalent to affixing it to the house. They did not claim that the contents of the book were indecent.

The solicitor acting for the shopkeeper said that he had never heard a more fantastic suggestion. The clerk to the magistrates declared that he was not disposed to advise them that the display of the book was an advertisement, and that he would advise them that the word "affixed" meant precisely what it said. The solicitor, applying for dismissal of the summons with costs against the police, maintained that the shopkeeper should not suffer financial loss owing to the "crass stupidity" of the police in bringing the summons. The bench, however, in dismissing the summons refused to make an order for costs.

The law on indecent publication is very obscure and confused, but there seems little justification for an attempt to stretch it as far as this. The remark of the solicitor for the defence, that if it is illegal to place books of this nature in shop windows there is not a bookseller from London to Manchester who does not commit an offence practically every day, is irrefutable. The time has long gone by when any useful purpose could be served by attacking in this way even really obscene publications, let alone innocent ones on such subjects as venereal disease.

[1] *Manchester Guardian*, January 24, 1950.

# Universities and Colleges

## UNIVERSITY OF LONDON

The following appointments to the Senate for the period 1950–4 have been made: *Convocation—Medicine*, Sir Alexander Fleming, F.R.S. *Faculty of Medicine*, Dr. E. R. Boland and Mr. J. B. Hunter. *General Medical Schools*, Sir Harold A. Boldero. Dr. C. F. Harris has been appointed a member of the Senate as one of the representatives of the General Medical Schools for the period 1950–2.

John Bernard Kinmonth, M.S., F.R.C.S., has been appointed to the University Readership in Surgery tenable at St. Bartholomew's Hospital Medical College, from June 1.

## UNIVERSITY OF BIRMINGHAM

The following appointments are announced: Deryk Darlington, M.B., Ch.B., to be Lecturer in Anatomy from April 1; B. S. B. Wood, B.M., B.Ch., M.R.C.P., D.C.H., to be Lecturer in Paediatrics and Child Health from March 1; A. Lasnitzki, M.Sc., M.D., to be Senior Research Fellow in Biochemistry (Cancer Research) from October 1, 1949.

## UNIVERSITY OF LEEDS

At a Congregation held on May 19 the honorary degree of D.Sc. was conferred on William Norman Pickles, M.D., M.R.C.P., Medical Officer of Health for Aysgarth Rural District Council.

Rupert Allan Willis, D.Sc., M.D., F.R.C.P., Director of the Pathology Department of the Royal Cancer Hospital, London, has been appointed Professor of Pathology in the University from October 1.

## UNIVERSITY OF SHEFFIELD

The following appointments are announced: *Demonstrators in Anatomy*, J. B. Parkin, M.B., Ch.B., and B. A. E. Johns, M.B., Ch.B., M.R.C.P. *Research Assistant in Medicine*, Margaret M. Platts, M.B., Ch.B. *Junior Graves Research Fellow*, G. Ansell, M.D., M.R.C.P. *Honorary Demonstrator (part-time) in Bacteriology*, J. C. Burne, M.B., Ch.B.

Dr. J. A. Kilpatrick has resigned from the post of lecturer in medicine, on returning to New Zealand, and Dr. R. O'Rahilly as lecturer in anatomy, on taking up a travelling scholarship to the U.S.A.

## ROYAL COLLEGE OF SURGEONS OF ENGLAND

The following lectures will be delivered at the College (Lincoln's Inn Fields, London, W.C.) at 5 p.m. each day: Tuesday, June 6, Arnott Demonstration by Mr. F. S. Gorrill, "The Anatomy and Physiology of the Spleen"; Wednesday, June 14, Ophthalmology Lecture by Professor Leon Stone, "Development of Normal and Reversed Vision in Transplanted Eyes"; Thursday, June 15, Hunterian Lecture by Professor S. A. Henry, "Cutaneous Cancer in Relation to Occupation"; Monday, June 19, Moynihan Lecture by Professor F. M. Burnet, F.R.S., "The Natural History of Surgical Infection"; Thursday, June 22, Erasmus Wilson Demonstration by Mr. P. H. Mitchiner, "Dry Bones"; Tuesday, June 27, Hunterian Lecture by Dr. Arthur W. Allen, "Modern Trends in Colonic Surgery." The lectures are open to all those attending courses in the College and to all other medical practitioners, dental surgeons, and advanced students.

At a meeting of the Council of the College, held on May 11, with Sir Cecil Wakeley, President, in the chair, Dr. David Slome was appointed Professor of Applied Physiology in the College.

The Cecil Joll Prize for 1950 was awarded to Sir Thomas Dunhill for his outstanding work on surgery of the thyroid.

The following hospitals were recognized under paragraph 23 of the Fellowship regulations: Aberystwyth–Cardiganshire General Hospital, senior house-surgeon (for six months only); Derbyshire Royal Infirmary, ear, nose and throat registrar (additional post); Salford Royal Hospital, two senior surgical registrars, two surgical registrars, three junior surgical registrars, one registrar, ear, nose and throat; Morriston Hospital, Swansea, three registrars and (for six months only) house-surgeon for general surgery, house-surgeon for neurosurgery, and house-surgeon for orthopaedics.

Diplomas of Membership were granted to the 204 successful candidates whose names were printed in the report of the meeting of the Royal College of Physicians of London in the *Journal* of May 13 (p. 1150).

Diplomas of Fellowship in Dental Surgery were granted to the following successful candidates: P. F. B. Gillett, M.R.C.S., L.R.C.P., D. C. Smith, G. E. Ray, E. H. Cooper, A. Karim, A. D. McIntyre, A. W. D. Cowan, H. D. Penney.

## ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a meeting of the Royal College of Surgeons of Edinburgh held on May 17, with Mr. W. Quarry Wood, President, in the chair, the following candidates, having passed the requisite examinations, were admitted Fellows: K. S. Alam, A. D. R. Batchelor, B. B. Bhattacharyya, A. L. De P. Carnegie, H. V. Corbett, A. S. Davidson, I. B. Faris, F. M. Fattouh, C. F. G. Fourie, E. F. B. Hamilton, A. P. Hayward, N. L. Kalle, J. Lister, R. S. McCrea, A. G. O'Malley, R. G. Parker, I. R. Ross, L. M. Satchwell.

## ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

Through the generosity of the Leverhulme Trust the Council of the College is in a position to award scholarships for the purposes of research into problems connected with obstetrics and/or gynaecology. The scholarships may be held simultaneously with another appointment if, in the opinion of the Council, sufficient time is available for research. Regulations and forms of application can be obtained from the secretary of the College, 58, Queen Anne Street, London, W.1. The last day for receiving applications on the prescribed form is July 1.

The National Corporation for the Care of Old People supports three "Darby and Joan" clubs at Croydon, Lewisham, and Streatham. The clubs are open six days a week, and each has 1,000 members or more on its books. They provide a sitting-room and recreation space, and meals at reasonable prices. In the second National Report of the Corporation the governors state that they cannot support similar ventures without discovering if it is possible for voluntary organizations to find the heavy annual maintenance costs. They feel that these clubs can do much towards helping to solve, at least temporarily, the difficulties arising from lack of housing accommodation, but a higher proportion of voluntary assistance is called for.

# Medical News

### Osler Medal Award

The Osler Memorial Medal for 1950 has been awarded by the University of Oxford to Sir Ernest L. Kennaway, F.R.S., Honorary Fellow of New College, Oxford, and Professor Emeritus of Experimental Pathology in the University of London. The award is in the form of a bronze medal which is awarded once in every five years to the Oxford medical graduate who, in the opinion of the board of awarders, has made the most valuable contribution to the science, art, or literature of medicine and who has not previously received the medal.

### British Association of Physical Medicine

The British Association of Physical Medicine held its annual general meeting at the Royal College of Surgeons on May 12. The president, Lord Horder, was in the chair. After the meeting Dr. Frank Krusen, of the Mayo Clinic, read a paper on the work of the Bernard Baruch Committee in Physical Medicine and Rehabilitation. Lord Horder also took the chair at the annual dinner, which was held in the library of the College of Surgeons. Lord Horder proposed the toast of the guests, to which Sir Cecil Wakeley, P.R.C.S., responded. Dr. Frank Krusen proposed the toast of the British Association of Physical Medicine, to which Dr. William Tegner, secretary of the association, responded. It was announced at the dinner that an International Association of Physical Medicine had been formed, and Dr. Krusen had been elected interim president and Dr. Philippe Bauwens interim secretary pending the calling of a congress.

### St. John Ambulance Brigade

A conference of surgeons was held at the Queen Hotel, Harrogate, under the supervision of the Deputy Surgeon-in-Chief, Mr. F. H. Edwards. Dr. Donald Towle lectured on the effects of atomic explosions on human beings, with suggested lines of treatment. There were also papers on the problems of teaching laymen the principles of child welfare and home nursing, by Dr. Muriel Frazer, of Belfast, and Dr. Maxwell Reekie, of Manchester, assisted by Miss M. E. Dean. A similar conference will be held in April, 1951, either at Buxton or Harrogate.

### Queues at the Hospitals

Speaking at the first annual general meeting of the United Sheffield Hospitals on May 12, Sir Ernest Rock Carling drew attention to the serious situation which existed because many people were unable to obtain the hospital treatment they required. The waiting-list of the United Sheffield Hospitals was nearly 8,000 at December 31, 1949. This was not a problem to be solved by the United Sheffield Hospitals but by the whole community. The queue of 8,000-strong at the front door should be tackled in two ways: first, by providing greater in-patient accommodation, and, secondly, by reducing the number of people joining the queue. "It is difficult to get certain classes of patients out of the hospital because there are not services providing suitable places into which they can go on discharge. It applies perhaps most of all to the elderly and infirm. In my opinion there is a need for 2,000 homes in this country with 30 or 40 beds in each where comfort could be found by the elderly and infirm." The task of reducing the number of patients presenting themselves at the front door was in the hands of the general practitioner service, which would be greatly assisted in its efforts by the introduction of health centres.

### Wills

Dr. Dudley George Greenfield, of Rushden, Northants, a former member of Council of the B.M.A., left £35,226; Dr. Thomas Joseph Kirk, of Bournemouth, £11,509; Dr. Alexander George Gibson, formerly consulting physician, Radcliffe Infirmary, Oxford, £18,336; and Mr. Reginald Ernest Bickerton, £1,198.

## COMING EVENTS

### British Medical Students Association

The following arrangements have been made for the week May 26—June 2. *Aberdeen.*—May 30 (Medical Society): Lecture by Dr. Alexander Lyall, honorary president. *University of Durham.*—May 26: Lecture by Mr. Geoffrey Armitage on "Without Frontiers." *Oxford University Medical Society.*—May 30: Lecture by Professor Mackintosh on "What is a Hospital for?"

### British Association of Physical Medicine

A short course of lectures on the various aspects of physical medicine, suitable for candidates preparing for Part II of the Diploma in Physical Medicine, has been arranged on Tuesdays and Thursdays from June 1 to July 4, inclusive, at 5 p.m. Further details can be obtained from the honorary secretary, British Association of Physical Medicine, 45, Lincoln's Inn Fields, London, W.C.2.

### Queen's University Club, London

The Queen's University Club, London, will hold its 20th annual Spring dinner and dance at the May Fair Hotel, London, W., on Thursday, June 1, at 7 for 7.30 p.m. All Queen's men and women are invited to attend.

### Scottish Registrars' Meeting

A general meeting of the Registrars' Association, South-eastern Region, Scotland, will be held at B.M.A. Scottish House, Drumsheugh Gardens, Edinburgh, on Thursday, June 1, at 8 p.m. Registrars of all grades serving in the region are requested to attend.

### Simpson-Smith Memorial Lecture

Sir James Learmonth will deliver the third Alex. Simpson-Smith Memorial Lecture at the West London Hospital Medical School on Wednesday, June 7, at 8.30 p.m. His subject is "The Surgery of the Sympathetic Nervous System." Admission is by ticket only, obtainable from the Dean of the school.

### Medical Women's Federation

The London Association of the Medical Women's Federation has arranged a conducted tour of Glaxo Laboratories, Greenford, on Thursday, June 8. A coach will leave B.M.A. House (Tavistock Square, London, W.C.) at 1.45 p.m. The number of persons that can be shown over the laboratories in one party is limited and admission is by ticket only, obtainable from the honorary secretary, Dr. Margaret M. C. Louden, 5, Wapping Pierhead, London, E.1, before June 3. If applications exceed the limit a second meeting will be arranged in the near future.

### Oxford Graduates' Medical Club

The summer dinner of the Oxford Graduates' Medical Club will be held at Brasenose College, Oxford, on Friday, June 30, at 7.30 for 8 p.m., when the chair will be taken by Sir Henry Tidy. All men who are Oxford graduates, studying or practising medicine, are eligible for membership, and it is hoped that there will be a good attendance. Accommodation is restricted, making it impossible to allow guests on this occasion. Applications for tickets should be made as soon as possible, and not later than June 9, to the honorary secretary, Mr. E. G. Tuckwell, F.R.C.S., 73, Harley Street, London, W.1. Dinner jackets will be worn. The cost of the dinner is 30s., inclusive of wine with the meal.

### The Horse Shoe Club

At 5 p.m. on Thursday, June 15, at the Medical Society of London, 11, Chandos Street, Cavendish Square, London, W.1, a meeting will be held to consider future activities of the Horse Shoe Club, which was started in 1932 to promote the exchange of doctors between the U.S.A. and this country and to give American doctors hospitality on their arrival here. It is hoped that former members and others interested in these objects will come, and especially those who have recently visited the U.S.A. Dr. Geoffrey Bourne will be in the chair.

## SOCIETIES AND LECTURES

A fee is charged for attending lectures marked ●. Application should be made first to the institution concerned.

### Friday

CAMBRIDGE MEDICAL SOCIETY.—At Addenbrooke's Hospital, Cambridge, May 26, 2.30 p.m., "*The Body-image*," by Dr. Macdonald Critchley.

### Saturday

NUTRITION SOCIETY.—At London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, W.C., May 27, 10.30 a.m., annual general meeting and open scientific meeting.

### Monday

EDINBURGH UNIVERSITY.—At Physiology Lecture Theatre, University New Buildings, Teviot Place, Edinburgh, May 29, 5 p.m., "*The Way of the Investigator*," by Dr. Douglas Guthrie.

### Tuesday

EDINBURGH POSTGRADUATE BOARD FOR MEDICINE.—At Anatomy Lecture Theatre, University New Buildings, Edinburgh, May 30, 5 p.m., "*Staphylococcal Infection in Childhood with Special Reference to Osteomyelitis*," by Professor J. C. Spence.

INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 30, 5 p.m., "*Erythemato-squamous Eruptions*," by Dr. H. J. Wallace.

INSTITUTE OF OPHTHALMOLOGY (UNIVERSITY OF LONDON), Judd Street, London, W.C.—May 30, 5.30 p.m., "*Surgical Treatment of Squint*," by Mr. T. K. Lyle.

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, London, W.C.—May 30, 5 p.m., "*The Physiology of the Bone*," Arnott Demonstration by Mr. F. S. Gorrill.

ROYAL EYE HOSPITAL (KING'S COLLEGE HOSPITAL GROUP), St. George's Circus, London, S.E.—May 30, 5 p.m., "*Surgery of the Iris*," by Mr. T. M. Tyrrell.

WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, Paddington, W.—May 30, 5 p.m., "*Factors that Determine the Initial Stages of Infection*," by Dr. A. A. Miles.

### Wednesday

INSTITUTE OF DERMATOLOGY, Lisle Street, Leicester Square, London, W.C.—May 31, 5 p.m., "*Histology*," by Dr. H. Haber.

ROYAL EYE HOSPITAL (KING'S COLLEGE HOSPITAL GROUP), St. George's Circus, London, S.E.—May 31, 5.30 p.m., "*Ophthalmic Neurology*," by Mr. L. H. Savin.

UNIVERSITY COLLEGE (Anatomy Theatre), Gower Street, London, W.C.—May 31, 5.30 p.m., "*The Biochemical Approach to Biological Organization*," by Professor Ernest Baldwin.

### Thursday

FACULTY OF HOMOEOPATHY.—At Royal London Homoeopathic Hospital, Great Ormond Street, London, W.C., June 1, 5 p.m., "*The Mysterium of Prescribing*," by Dr. Karl Konig.

HONYMAN GILLESPIE LECTURES.—At Anatomy Theatre, University New Buildings, Teviot Place, Edinburgh, June 1, 5 p.m., "*The Acid Secretion of the Stomach*," by Professor C. F. W. Illingworth.

INSTITUTE OF NEUROLOGY: NATIONAL HOSPITAL, Queen Square, London, W.C.—June 1, 5 p.m., "*Specular Hallucinations ('Heautoscopy')*," by Professor J. Lhermitte (Paris).

INSTITUTE OF OPHTHALMOLOGY (UNIVERSITY OF LONDON), Judd Street, London, W.C.—June 1, 5.30 p.m., "*The Corneal Dystrophies*," by Professor A. Sorsby.

MIDDLESEX HOSPITAL MEDICAL SOCIETY.—At Middlesex Hospital (Library), London, W., June 1, 8.30 p.m., annual special meeting and address by Sir James Paterson Ross; exhibition, the Middlesex Hospital, 1745–1950.

LONDON COUNTY MEDICAL SOCIETY.—At Highwood Hospital, Brentwood, Essex, June 1, 3 p.m., clinical meeting.

LONDON UNIVERSITY.—At St. Mary's Hospital Medical School, Paddington, London, W., June 1, 5 p.m., "*Hormones of the Anterior Hypophysis*," by Professor H. M. Evans (University of California).

ROYAL EYE HOSPITAL (KING'S COLLEGE HOSPITAL GROUP), St. George's Circus, London, S.E.—June 1, (1) 4.15 p.m., "*Methods of Examination*," by Mr. C. M. Shafto; (2) 5 p.m., "*Ocular Palsy*," by Dr. S. Nevin.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL, Hyde Park Corner, London, S.W.—June 1, 4.30 p.m., "*Psychiatry*," lecture-demonstration by Dr. D. Curran.

### Friday

HEBERDEN SOCIETY.—At B.M.A. House, Tavistock Square, London, W.C., June 2, 10 a.m., "*The Rheumatic Diseases as Diseases of Adaptation*," Heberden Oration by Professor Hans Selye (Montreal). (See Saturday also.)

LONDON UNIVERSITY.—At St. Mary's Hospital Medical School, Paddington, London, W., June 2, 5 p.m., "*Hormones of the Anterior Hypophysis*," by Professor H. M. Evans (University of California).

MAIDA VALE HOSPITAL FOR NERVOUS DISEASES MEDICAL SCHOOL, Maida Vale, London, W.—June 2, 5 p.m., clinical neurological demonstration, by Dr. Redvers Ironside.

ROYAL EYE HOSPITAL (KING'S COLLEGE HOSPITAL GROUP), St. George's Circus, London, S.E.—June 2, 4.15 p.m., "*Artificial Eyes*," by Mr. G. C. Pritchard.

● WEST LONDON MEDICO-CHIRURGICAL SOCIETY.—At Royal College of Surgeons of England, Lincoln's Inn Fields, London, W.C., June 2, 7.30 for 8 p.m., annual banquet.

WHIPPS CROSS HOSPITAL MEDICAL SOCIETY, Whipps Cross Hospital, London, E.—June 2, 8.30 p.m., "*Chemotherapy*," by Dr. F. C. O. Valentine.

### Saturday

HEBERDEN SOCIETY.—At B.M.A. House, Tavistock Square, London, W.C., June 3, 10 a.m., "*The Rheumatic Diseases as Diseases of Adaptation*," Heberden Oration by Professor Hans Selye (Montreal). (See Friday also.)

## APPOINTMENTS

David Slome, Ph.D., M.B., Ch.B., has been appointed to the Chair of Applied Physiology at the Royal College of Surgeons of England from October 1.

Dr. Slome graduated from the University of Capetown in 1931. He obtained his M.A. in 1927 and Ph.D. in 1930, subsequently winning the Hallett Prize. Dr. Slome has been a demonstrator in physiology at St. Bartholomew's Hospital Medical College and a lecturer in physiology at the Middlesex Hospital Medical School. He is at present reader in physiology in the University of London. He has also been a Leverhulme Research Scholar and a Mackenzie Mackinnon Research Scholar of the Royal College of Surgeons of England and has delivered an Arris and Gale Lecture.

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—*Consultant Venereologist in Stamford, Peterborough, and King's Lynn Area*, N. A. Ross, M.B., Ch.B., D.P.H. *Assistant Chest Physician (Senior Registrar) in East Suffolk and Ipswich Area*, A. H. C. Couch, M.D., M.R.C.P., D.C.H.

HAY, ARTHUR WILLIAM, M.B., B.S., D.P.H., Senior Assistant Medical Officer of Health, Middlesbrough.

HOSPITAL FOR SICK CHILDREN, Great Ormond Street, London, W.C.—*House-physician (Junior Registrar Grade)*, P. J. N. Cox, B.M., B.Ch., M.R.C.P., D.C.H. *House-surgeon (Junior Registrar Grade)*, J. V. Coyle, M.B., Ch.B. *Assistant Medical Registrars (Registrar Grade)*, J. C. Macaulay, M.B., B.S., M.R.C.P., D.C.H., Joan P. D'Arcy, M.B., B.Ch., D.C.H. *Resident Aural Registrar (Registrar Grade)*, I. Crawford Jones, M.R.C.S., L.R.C.P. *Medical Registrar and Pathologist (Senior Registrar Grade)*, D. N. Lawson, M.D., M.R.C.P.

LIVERPOOL REGIONAL HOSPITAL BOARD.—*Visiting Consultant Assistant General Surgeon to hospitals in Ormskirk Group*, C. T. A. Burgess, F.R.C.S. *Whole-time Tuberculosis Medical Officers*, R. M. White, M.B., Ch.B., D.P.H. (for Warrington area) and J. Baxter, M.B., Ch.B., D.P.H. (for Wallasey area).

ODDIE, J. A., M.B., B.S., Assistant Medical Officer, East Anglian Regional Hospital Board.

VER HEYDEN DE LANCEY, CORNELIUS, M.D., D.D.S., LL.B., L.R.C.P., L.M.S.S.A., B.D.Sc., L.D.S. R.C.S.Ed., Advocate of the Royal Court, Jersey, Channel Islands.

## BIRTHS, MARRIAGES, AND DEATHS

### BIRTHS

**Devlin.**—On April 23, 1950, to Dr. Audrey (formerly Conyngham), wife of Dr. Henry R. T. Devlin, Clovergates, Tresahar Road, Falmouth, Cornwall, a daughter—Melissa.

**Mack.**—On May 20, 1950, at the Avenue Hospital, Bridlington, to Maureen (formerly Twidle), M.B., Ch.B., wife of Edward W. Forsyth Mack, M.R.C.S., L.R.C.P., a son.

**Ritchie.**—On May 14, 1950, at Ashleigh, Newcastle-upon-Tyne, to Molly (formerly Hudson), M.B., Ch.B., wife of Lewis W. Ritchie, M.B., Ch.B., D.A., a daughter.

### DEATHS

**Duffin.**—On April 22, 1950, John Duffin, M.B., Ch.B., of 15, Teignmouth Gardens, Perivale, Middlesex, aged 59.

**Gordon.**—On May 17, 1950, at Threeways, Tranwell Wood, Morpeth, Northumberland, William Ingram Gordon, M.B., Ch.B.

**Greig.**—On May 18, 1950, at 3, Lansdowne Road, Croydon, Surrey, David Low Greig, M.R.C.S., L.R.C.P., D.M.R.E., aged 55.

**Salt.**—On May 17, 1950, at St. Modwen's Nursing Home, Burton-upon-Trent, Edmund Cecil Salt, M.B., Ch.B., aged 78.

**Thomson.**—On May 19, 1950, Charles Thomson, M.B., C.M., Lieutenant-Colonel, I.M.S., retired, of 36, Oakcroft Road, London, S.E., aged 80.

**Wall.**—On May 19, 1950, at a Bournemouth nursing-home, Frank Wall, C.M.G., M.R.C.S., L.R.C.P., Colonel, I.M.S., retired, of 30, Milton Road, Bournemouth, aged 82.

During a British Council lecture tour in Cyprus between April 12 and 24 Dr. J. L. Lovibond, assistant physician to the Westminster Hospital, visited hospitals and gave demonstrations on the use of the cardiograph in various parts of the island. His tour was arranged in co-operation with the Director of Medical Services, Cyprus, and he lectured on special diagnostic tests in cardiovascular disease, the modern treatment of cardiac disease, the interpretation of electrocardiograms, and hypertension.

No. 18

# INFECTIOUS DISEASES AND VITAL STATISTICS

We print below a summary of Infectious Diseases and Vital Statistics in the British Isles during the week ended May 6.

Figures of Principal Notifiable Diseases for the week and those for the corresponding week last year, for: (a) England and Wales (London included). (b) London (administrative county). (c) Scotland. (d) Eire. (e) Northern Ireland.

*Figures of Births and Deaths, and of Deaths recorded under each infectious disease, are for:* (a) The 126 great towns in England and Wales (including London). (b) London (administrative county). (c) The 16 principal towns in Scotland. (d) The 13 principal towns in Eire. (e) The 10 principal towns in Northern Ireland.

A dash — denotes no cases; a blank space denotes disease not notifiable or no return available.

| Disease | 1950 (a) | (b) | (c) | (d) | (e) | 1949 (Corresponding Week) (a) | (b) | (c) | (d) | (e) |
|---|---|---|---|---|---|---|---|---|---|---|
| Meningococcal infection | 34 | 5 | 18 | 2 | 2 | 32 | 1 | 18 | 3 | 2 |
| Deaths | | — | 1 | | | | — | — | | |
| Diphtheria | 41 | 2 | 17 | 2 | 5 | 98 | 20 | 20 | 6 | 8 |
| Deaths | — | — | 1 | — | — | 1 | — | — | — | — |
| Dysentery | 341 | 6 | 89 | 1 | — | 38 | 4 | 35 | 1 | 15 |
| Deaths | | — | | | — | | | | — | — |
| Encephalitis, acute | 2 | 1 | — | — | — | — | — | 1 | — | — |
| Deaths | | — | | | | | — | | | |
| Erysipelas | | | 20 | 6 | 5 | | | 21 | 7 | 4 |
| Deaths | | | | | | | | | | |
| Infective enteritis or diarrhoea under 2 years | | | | 17 | | | | | 37 | |
| Deaths | 18 | | 3 | 1 | — | 26 | 3 | 3 | 2 | 1 |
| Measles* | 6,317 | 141 | 467 | 147 | 238 | 11,436 | 1541 | 513 | 255 | 171 |
| Deaths† | | | — | 1 | — | | | 1 | 1 | — |
| Ophthalmia neonatorum | 29 | 3 | 7 | | — | 44 | 2 | 6 | — | 1 |
| Deaths | | | | | | | | | | |
| Paratyphoid fever | 7 | 3 | — | | — | 1 | — | 1 (B) | — | — |
| Deaths | — | | — | | — | — | — | — | — | — |
| Pneumonia, influenzal | 534 | 20 | 6 | — | 7 | 453 | 21 | 13 | 9 | 15 |
| Deaths (from influenza)‡ | 24 | 6 | 1 | 4 | 1 | 39 | 2 | 2 | 1 | — |
| Pneumonia, primary | | | 156 | ¶ | | | | 162 | 33 | |
| Deaths | 152 | 17 | | 11 | 5 | 176 | 22 | | 9 | 10 |
| Poliomyelitis, acute | 25 | 2 | — | 2 | 4 | 14 | 1 | — | 2 | — |
| Deaths§ | 2 | — | | — | | — | — | | | |
| Puerperal fever | | — | 6 | | | | — | 10 | | |
| Deaths | | | | | | | | | | |
| Puerperal pyrexia‖ | 87 | 8 | 11 | | | 80 | 7 | 8 | 1 | — |
| Deaths | | | | | | | — | | | |
| Relapsing fever | — | — | | | — | — | — | | | — |
| Deaths | | | | | | | | | | |
| Scarlet fever | 1,267 | 88 | 130 | 83 | 71 | 785 | 66 | 145 | 60 | 29 |
| Deaths† | | | — | — | — | | | — | — | — |
| Smallpox | 3 | — | — | | — | — | — | — | — | — |
| Deaths | | | | | — | | | | — | — |
| Typhoid fever | 3 | — | 1 | 2 | — | 6 | 1 | — | 2 | — |
| Deaths | — | — | — | — | — | 1 | — | — | — | — |
| Typhus fever | — | — | — | — | — | — | — | — | — | — |
| Deaths | | | | | — | | | | — | — |
| Whooping-cough | 3,229 | 167 | 321 | 64 | 49 | 2,905 | 167 | 249 | 153 | 88 |
| Deaths | 5 | 1 | — | 2 | — | 9 | — | 1 | 2 | — |
| Deaths (0–1 year) | 271 | 36 | 36 | 29 | 8 | 261 | 33 | 32 | 30 | 18 |
| Deaths (excluding stillbirths) | 4,942 | 715 | 599 | 230 | 133 | 4,657 | 670 | 541 | 214 | 125 |
| Annual death rate (per 1,000 persons living) | | | 12·0 | | | | | 10·9 | 13·3 | |
| Live births | 7,725 | 1272 | 932 | 528 | 230 | 8,200 | 1394 | 1039 | 488 | 250 |
| Annual rate per 1,000 persons living | | | 18·7 | | | | | 20·8 | 30·2 | |
| Stillbirths | 177 | 23 | 22 | | | 212 | 32 | 37 | | |
| Rate per 1,000 total births (including stillborn) | | | 23 | | | | | 34 | | |

* Measles is not notifiable in Scotland, and the returns are therefore an approximation only.

† Deaths from measles and scarlet fever for England and Wales, London (administrative county), will no longer be published.

‡ Includes primary form for England and Wales, London (administrative county), and Northern Ireland.

§ The number of deaths from poliomyelitis and polio-encephalitis for England and Wales, London (administrative county), are combined.

‖ Includes puerperal fever for England and Wales and Eire.

¶ Primary pneumonia no longer notifiable in Eire.

# EPIDEMIOLOGICAL NOTES

## Discussion of Table

In *England and Wales* increases were recorded in the notifications of scarlet fever 143 and dysentery 66, and decreases were reported for measles 63, whooping-cough 47, and diphtheria 14.

The chief feature of the returns for this week was the number of notifications of diphtheria, which was the lowest ever recorded, being 11 below the previous lowest total recorded 36 weeks ago. Of the 41 cases 12 were notified in Lancashire and 9 in Durham. The towns with the largest numbers of notifications were Liverpool C.B. with 6 and Birmingham C.B. with 5.

The largest decreases in the notifications of measles were Lancashire 118, Kent 116, Leicestershire 96, London 62, and Essex 50, and the largest increases were Durham 196, Northumberland 69, and Denbigh 57. Only small rises occurred in the notifications of scarlet fever, the largest being increases of 23 in Kent and Staffordshire. The greatest fluctuations in notifications of whooping-cough were an increase in Lancashire of 34 and a decrease in Lincolnshire of 39.

The largest returns of dysentery were Yorkshire West Riding 100 (Sheffield C.B. 37, Bradford C.B. 31); Lancashire 72 (Failsworth U.D. 24, Manchester C.B. 22, Warrington C.B. 14); Durham 53 (Stanley U.D. 15, South Shields C.B. 12, Blaydon U.D. 7, West Hartlepool C.B. 6); Gloucestershire 26 (Cheltenham R.D. 20); Essex 21 (Ilford M.B. 18); and Northumberland 19 (Newcastle-upon-Tyne C.B. 9).

In *Scotland* infectious diseases were less prevalent during the week, the largest declines in the number of notifications being measles 145, whooping-cough 107, dysentery 93, scarlet fever 33, and acute primary pneumonia 16. Eight cases of dysentery were notified in Clackmannan county, compared with 53 in the preceding week. The other important centres of dysentery were Glasgow with 47 notifications, Dundee with 15, and Edinburgh with 10.

In *Eire* increases were reported in the number of notifications of measles (37) and scarlet fever (14), while a decrease was recorded for whooping-cough (39). The rises in the incidence of measles and scarlet fever were mainly due to the experience of Dublin C.B., where the increases in notifications were 23 and 20 respectively. Forty-nine of the 64 cases of whooping-cough were notified in Dublin C.B.

In *Northern Ireland* a further fall of 38 in the number of notifications of measles was the only variation in the trends of infectious diseases. The largest local variations in the returns of measles was a decrease of 33 in Belfast C.B. and an increase of 18 in Londonderry county.

## Week Ending May 13

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 1,322, whooping-cough 3,469, diphtheria 43, measles 7,278, acute pneumonia 502, acute poliomyelitis 22, dysentery 444, paratyphoid fever 11, typhoid fever 6.

---

The Minister of Health, according to a circular sent to hospitals, regards it as important both on general and on therapeutic grounds that a library service for patients should gradually be developed to a high standard in all hospitals. Many hospitals are already co-operating with the local public library or using facilities provided by the Order of St. John and the British Red Cross Society. The service required will vary from a small stock of books handled by part-time workers to what is almost a branch municipal library located in the hospital. No additional expenditure will be authorized. After June 30 the Order of St. John and the British Red Cross Society will make a charge for the library service of 5s. per annum per occupied bed, plus the salaries of any paid librarians engaged.

# Any Questions?

*Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.*

### "Dumping" Syndrome

**Q.**—*What is the right treatment for the "dumping" syndrome following partial gastrectomy? A patient, aged 29, who had a severe duodenal ulcer for 10 years, underwent a partial gastrectomy 18 months ago. He seemed much improved, but had a lot of "dumping," and he continued to have hunger pains. There have been two fairly severe attacks of melaena and haematemesis in the past three months. What is the treatment? Vagotomy has been suggested—is this advisable?*

**A.**—The "dumping" syndrome appears to be produced by food passing too quickly into the jejunum, particularly if it is too cold or too sugary. Alvarez recommends the following regimen: (1) Treat the nervous state by sedation. (2) Avoid fluids at meal-times; start each meal with a piece of toast "to plug the hole." (3) Eat slowly; take food at body temperature and keep it fairly isotonic by avoiding too much sugar. (*Gastroenterology*, 1949, **13**, 212). In this case, the operation does not appear to have had the desired effect of depressing the tendency to form further ulcers, and the most likely cause of the haemorrhage in the past three months is jejunal ulceration. Vagotomy has been recommended for such cases, but the evidence is still not entirely satisfactory, and the operation of choice is really a higher gastrectomy.

### Glandular Fever and Chronic Infectious Lymphocytosis

**Q.**—*Is it possible for glandular fever to produce numerous relapses, or to show itself as a prolonged low-grade pyrexia? What is the value of the differential count and the Paul–Bunnell test in diagnosis? Is there any way of terminating the prolonged pyrexia? Is there any literature on this subject? I ask this question because I have seen several cases of children aged from 4 to 14 years with a prolonged low-grade pyrexia, in some cases for over a year. One child had a relapse two years after the initial illness. Most of these cases have had enlarged glands, usually cervical, and the spleen has been palpable at some stage of the illness. Occasionally the liver has been enlarged. A few have shown raised mononuclear counts, ranging from 5 to 16%, but only one has given a positive Paul–Bunnell test.*

**A.**—It is possible for relapse to occur in glandular fever, although it is not met in more than 4 or 5% of cases. Recrudescence is more common, particularly when the patient is allowed to resume normal activity before he has completely recovered. In such instances the period of convalescence may be prolonged to several months, during which time the enlarged glands remain palpable. Glandular fever requires for its diagnosis either the characteristic cytological changes in the blood or the presence of a Paul–Bunnell test positive in a titre of 1:64 or higher. The blood changes may sometimes be delayed for a week or more after the onset, and, in the leucopenic variety, may not be striking. The Paul–Bunnell test is positive in a diagnostic titre in about 80% of cases, but often not before the tenth day of the disease; the reaction usually remains positive for two or three months and occasionally persists for a year.

The cases described are perhaps more suggestive of "chronic infectious lymphocytosis" than of glandular fever. In this disorder a low grade pyrexia, often persisting for many months, follows a mild upper respiratory tract infection and is associated with moderate lymphocytosis. Glandular fever has been well reviewed by Bernstein (*Medicine*, 1940, **19**, 85) and Contratto (*Arch. intern. Med.*, 1944, **73**, 449). Infectious lymphocytosis was described by Smith (*Amer. J. Dis. Child.*, 1941, **62**, 231).

### Bovine Type of Pulmonary Tuberculosis

**Q.**—*What is the incidence, in various countries, of the bovine type of pulmonary tuberculosis? Could you comment on the epidemiological aspects of the condition in relation to causation and prevention?*

**A.**—Bovine tuberculosis of the lungs is now recognized as being comparatively common, and it has been shown to run a course identical with that of pulmonary tuberculosis caused by human tubercle bacilli. It has been calculated that, of deaths due to respiratory tuberculosis, bovine infection accounts for 1% in Wales, 1.7% in England, and 7% in Scotland. These deaths are more common in rural areas. An incidence of 40% of bovine pulmonary tuberculosis has been reported from rural areas in Denmark, compared with 3% in urban districts. Similar figures have been reported from other countries. Bovine pulmonary tuberculosis is common in those who attend infected cows, and infection by inhalation of the bovine bacillus from cow to man and from man to man has been demonstrated. Prevention can best be achieved by eradicating bovine tuberculosis from cattle.

### Pregnancy and Thyroid Abnormalities

**Q.**—*A patient of mine, a cretin, has become pregnant. She is healthy and intelligent and has for some years taken thyroid gr. 3 (0.2 g.) daily. How do I estimate her thyroid requirements during the coming months? Am I likely to encounter any special difficulties?*

**A.**—Adult cretinism is relatively rare, and pregnancy in a cretin still more rare, although H. W. Wallenberg reported the case of a cretin who became pregnant three times (*Med. Klin.*, 1922, **18**, 144). The case referred to in this question, therefore, is of clinical interest. Associated facts in relation to this problem are as follows. Women in goitre areas who have failed to become pregnant, or who have had abortions, have nevertheless had successful pregnancies when removed from the goitre areas. Patients with thyrotoxicosis, inadequately treated, tend to become pregnant less frequently than normal women, and tend to have miscarriages, premature labours, and stillbirths. Modern treatment avoids these complications, and the general rule is to treat the thyrotoxicosis rather than the pregnancy. As regards the thyrotoxic mother, the symptoms may improve during early and middle pregnancy, and may become worse towards the time of parturition or after it. Physiologically there appears to be an increased demand on the thyroid gland during pregnancy, and some temporary physiological enlargement is not uncommon.

As to the original question, it would appear that the normal maintenance dose of gr. 3 of thyroid daily should be continued. Monthly estimations of the basal metabolic rate and the blood cholesterol might indicate the need for a slight increase in this dosage, but this is unlikely and probably unnecessary. An excess of thyroid above physiological requirements is dangerous, as tending to miscarriage. With a maintenance dose it seems unlikely that any special difficulty should be encountered. Naturally the child will have to be carefully observed in case there is a congenital absence of the thyroid gland or in case the thyroid gland has been temporarily depressed in function by the administration of thyroid to the mother during pregnancy.

### Scarlet Fever and Infective Hepatitis

**Q.**—*Is there any relation between scarlet fever and infective hepatitis? A little girl contracted scarlet fever and was kept in her own home for a month. Her mother nursed her, and in about two weeks developed otorrhoea. About five weeks later the father had infective jaundice, and so had the grandmother. All live in the same house.*

**A.**—Any aetiological connexion between the streptococcal infection that affected the daughter and the mother and the infective hepatitis of the father and grandmother in this family is most unlikely. The mother almost certainly became infected from close contact with the child, whereas the other two members of the family seem to have been infected with the hepatitis

virus from some other common source. It may have been a visitor in the pre-jaundice stage of illness or a child with a mild missed attack. The mode of transfer of this condition is usually by direct droplet infection. The possibility of homologous serum jaundice transmitted by imperfectly sterilized needles would also have to be excluded.

### Wilson's Heart Block

**Q.**—*What is Wilson's heart block, and what are the main electrocardiographic features of this condition?*

**A.**—Wilson and his colleagues (*Amer. Heart J.*, 1934, 9, 472) gave a description of the electrocardiograms of three patients, all showing a special type of intraventricular block. They proved experimentally on a dog that the same configuration is produced when the right branch of the bundle of His is damaged. According to Wilson the electrocardiogram is characterized by a QRS interval measuring 0.12 second or more and by narrow R-deflections and broad S-deflections in lead I. In lead III there is a narrow Q or S deflection synchronous with S in the same lead. In cases in which the standard electrocardiogram is of this type precordial leads from the right side of the praecordium show a very late chief upstroke; precordial leads from the left side of the praecordium show an early chief upstroke approximately synchronous with the peak of R in lead I. These curves are strikingly similar to those obtained by the same method of leading after section of the right branch of the His bundle in dogs, and for this reason it is believed that electrocardiograms of the kind mentioned represent right bundle-branch block in man. In the view of these American workers there is much less difference in frequency "between clinical right and clinical left branch block than has heretofore been supposed."

### Ocular Effects of Dimethyl Sulphate

**Q.**—*Can any advice be given about the effects of dimethyl sulphate on the eyes. A patient recently complained that his eyes had been exposed to fumes of dimethyl sulphate in the course of making an artificial cream three weeks before. On examination there was pinkness of the eyes within the palpebral fissure. What is known about this condition and what treatment is suggested?*

**A.**—Dimethyl sulphate is a colourless or yellowish liquid giving off a greyish vapour at 50° C. It is used as a methylating or alcoholizing agent in industry, and it has an intense caustic action on the skin, and, by its fumes, on the mucous membranes, notably of the eyes and the respiratory tract. Dimethyl sulphate hydrolyses readily into methyl alcohol and sulphuric acid, and this is thought to be the explanation of its highly irritant action, although some authorities consider that the effects are due to the whole molecule. Kerato-conjunctivitis may occur some hours after the initial irritation of the conjunctiva, and total colour blindness and reduction of visual acuity have been described in one case. Degeneration of the endothelial cells seems not uncommon, and in general the severity of the eye lesions will depend on the duration and the extent of the exposure. The immediate first-aid treatment of a splash of any corrosive liquid in the eye is by "irrigation, irrigation, and then more irrigation." In the case of all liquid splashes, water should be used if the suitable antidote is not immediately available. A useful universal antidote to both acids and alkalis is a buffered phosphate solution:

| | |
|---|---|
| Monobasic potassium phosphate | 70 g. |
| Dibasic sodium phosphate ... | 180 g. |
| Dissolved in 850 ml. of distilled water. | |

### Opium Smokers

**Q.**—*Is it possible to detect opium smokers by examination of the urine or the blood?*

**A.**—The quantities of opium alkaloids absorbed by smoking opium are very small and their detection in blood or urine would be very problematical. The more recently developed absorption methods, however, are capable of detecting very small amounts of such substances as morphine, and might well be applied to the urine in such cases with some hope of success.

### Syphilis and Tuberculosis

**Q.**—*How is the course of pulmonary tuberculosis affected by syphilis, (a) contracted after the tuberculosis has become active, and (b) when tuberculosis occurs in an older untreated syphilitic subject?*

**A.**—Opinion is divided upon this subject, and little evidence of any value is to be found in the literature. The older writers thought that the combination of early syphilis and pulmonary tuberculosis was unfavourable to the latter, and that the lung lesions often progressed rapidly in patients with acute secondary syphilis. Tertiary syphilis, on the other hand, has even been said to exert a beneficial effect on pulmonary tuberculosis because of its tendency to produce fibrosis. It is obvious that the presence of any other disease is almost bound to have an unfavourable effect on pulmonary tuberculosis. But, in the writer's experience, concomitant syphilis in a tuberculous patient has been of little importance provided that anti-syphilitic treatment was instituted promptly.

## NOTES AND COMMENTS

**Promoting Lactation.**—Mr. T. H. BISHOP (London) writes: Professor R. S. Illingworth's letter of April 29 (p. 1020) brought to mind the following passage: "The Child, as soon as it is born, is taken from the Mother, and not suffered to suck till the Milk comes of itself; but is either fed with strange and improper Things, or put to suck some other Woman, whose Milk flowing in a full Stream, overpowers the new-born Infant, that has not yet learn'd to swallow, and sets it a coughing, or gives it the Hiccup: The Mother is left to struggle with the Load of her Milk, unassisted by the Sucking of the Child. Thus two great Evils are produced, the one a Prejudice to the Child's Health; the other, the Danger of the Mother's Life, at least the Retarding her Recovery; by causing what is called a Milk Fever; which has been thought to be natural, but so far from it, that it is entirely owing to this Misconduct. I am confident, from Experience, that there would be no Fever at all, were things managed rightly: Were the Child kept without Food of any kind, till it was hungry, which it is impossible it should be just after the Birth, and then applied to the Mother's Breasts; it would suck with Strength enough, after a few repeated Trials, to make the Milk flow gradually, in due Proportion to the Child's unexercised Faculty of swallowing, and the Call of it's Stomach. Thus the Child would not only provide for it's self the best of Nourishment, but by opening a free Passage for it, would take of the Mother's Load, as it increased, before it could oppress or hurt her; and therefore effectually prevent the Fever; which is caused only by the painful Distention of the lacteal Vessels of the Breasts, when the Milk is injudiciously suffered to accumulate." These words, contained in a pamphlet which was published anonymously in 1748, were written by William Cadogan (1711–97). His little work *AN Essay upon Nursing and the Management of Children, From their Birth to Three Years of Age, written in a Letter to one of the Governors of the Foundling Hospital*, did much to rectify the faulty methods of child management then in vogue, and to inaugurate a more rational approach to the subject. The above quotation is from the fourth edition, 1750, pp. 14–15, the first edition to bear the name William Cadogan of Bristol, M.D.

**Correction.**—In our account of the opening of the new Institute of the Medical Research Council at Mill Hill (May 13, p. 1133) there is an error. Sir Charles Harington is said to have referred to the Medical Research Council as the oldest of the research councils set up by the Government, "the others being the Council of Industrial Design and the Veterinary Research Council." The bodies to which Sir Charles actually referred were the Department of Scientific and Industrial Research and the Agricultural Research Council.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON, W.C.1. TELEPHONE: EUSTON 2111. TELEGRAMS: *Aitiology, Westcent, London.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs. Authors overseas should indicate on MSS. if reprints are required, as proofs are not sent abroad.

ADVERTISEMENTS should be addressed to the Advertisement Manager, B.M.A. House, Tavistock Square, London, W.C.1 (hours 9 a.m. to 5 p.m.). TELEPHONE: EUSTON 2111. TELEGRAMS: *Britmedads, Westcent, London.*

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the Association. TELEPHONE: EUSTON 2111. TELEGRAMS: *Medisecra, Westcent, London.*

B.M.A. SCOTTISH OFFICE: 7, Drumsheugh Gardens, Edinburgh.